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THE CHICAGO MEDICAL SCHOOL

QUARTERLY

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PROGRESS IN DIABETES

A Review*

PIERO P. FOA, M.D., Ph.D.**

Diabetes is a form of metabolic inflation; there is too much glucose going around. Some believe that this state of affairs is due to "overproduction" of glucose by the liver; others believe that it is due to "underutilization" by the peripheral tissues. For every recent paper supporting one theory, there appeared another lending comfort to the opposite camp and the long, loud, often bitter controversy is giving way to the belief that probably both overproduction and underutilization have some measure of responsibility in the production of diabetic hyperglycemia.

By means of hepatic catheterization and the determination of peripheral glucose artero-venous differences, Bondy and collaborators [1-3] found that the fasting glucose output of the liver of a normal person is 3.5 mg./kg./min., and that if the blood sugar is raised to 175 mg% by intravenous injection of glucose, the liver glucose output stops, and the peripheral A-V difference increases. In other words, as the blood sugar concentration rises, so does the peripheral utilization of glucose while glycogenolysis stops and the blood sugar is allowed to return to normal. In patients with diabetic ketosis the rate of liver glucose output is doubled, the fraction of it derived from protein is tripled, while the rate of peripheral glucose utilization is normal.

In contrast with these results, which support the theory of overproduction. Lipscomb and Crandall[4, 5] using a similar technique, found that following pancreatectomy the liver glucose output in the dog does not increase while the peripheral utilization decreases from 122 to 44 mg./kg./hr.

Chaikoff and collaborators[6-8] demonstrated that the rate of oxidation of C^{14}-labeled glucose to CO_2 is the same in normal and alloxan diabetic rats (40 to 50% of the injected dose in 6 hours). On the other hand, the rate of glucose oxidation in depancreatized dogs is reduced by 60%, being approximately 2 gms./hr. in the normal and 0.7 gm./hr. in the diabetic animal. Accordingly, in the normal dog, 51% of the expired CO_2 carbon is derived from glucose, whereas in the diabetic, only 11% derives from this source despite the fact that the body glucose pool is about 5 times as great in the diabetic as in the normal. These observations would seem to indicate that underutilization is very pronounced in dogs with pancreatic diabetes, but not in rats with alloxan diabetes.

The untreated diabetic excretes large quantities of glucose in the urine and if the utilization of glucose by the tissues were normal, as the overproduction theory demands, then the amount of glucose utilized (which can be calculated) plus the amount of glucose excreted (which can be measured) should equal the amount of glucose derived from the diet (which can be controlled) plus the amount derived from gluconeogenesis. If one calculates the glucose derived from protein on the basis of urinary ni-

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trogen, one finds that the amount is inadequate to account for all the gluconeogenesis necessary to even the score. Very significant amounts of glucose must therefore derive from fatty acids. Direct proof of this transformation had not been given until Chaikoff and collaborators[9] demonstrated that some of the radioactive carbon introduced into a fatty acid molecule could be found in the glucose produced by the liver of alloxan diabetic rats. Fatty acids, therefore, can be transformed into glucose although it is not clear to this writer if the amounts involved are of the magnitude required by the theory of overproduction.

It is probable that both peripheral "underutilization" and hepatic "overproduction" contribute to the diabetic syndrome, but the data available at the present time do not permit an accurate evaluation of their relative importance.

It's well known that when carbohydrate is not utilized (as in diabetes) or is not available (as in starvation) ketosis develops. Most people now believe that this happens because carbohydrate, which in normal conditions is oxidized preferentially, no longer competes with fatty acids for the available oxygen; fatty acids are metabolized in excess, and ketone bodies accumulate. When carbohydrate again becomes available, fat metabolism and ketone body production return to normal: thus carbohydrates would have a true antiketogenic action. The belief that fat can burn completely only in a "fire of carbohydrate" has only a historical interest. Discarded biological hypotheses, however, frequently reappear changed in the light of new knowledge. Recently Weinhouse[10] studied the oxidation of fatty acids labeled with C^{13} using rat liver slices. Some livers were obtained from fasted rats and contained little or no glycogen, some were obtained from well fed animals and were rich in glycogen. The author found that the presence of glycogen (or of added pyruvate) not only does not inhibit, but actually enhances the conversion of fatty acids to CO_2, decreasing the fraction converted to ketone bodies. The antiketone action of carbohydrates would be due, therefore, to a more complete combustion of fatty acids to water and Co_2 rather than to a decrease in fatty acid metabolism. Carbohydrates would have a ketolytic, not an antiketogenic action. According to Weinhouse, a carbohydrate may act by producing oxaloacetate (presumably through carboxylation of pyruvate), and oxaloacetate would promote the oxidation of the acetyl derivatives of fatty acid oxidation via the Krebs cycle. In the absence of carbohydrate and therefore of oxaloacetate, these acetyl groups would accumulate and condense into acetoacetate. In other words, carbohydrate metabolism would furnish the intermediary substance (or the "fire") necessary for the complete combustion of fatty acids via the Krebs cycle.

Somogyi[11] studied the peripheral glucose utilization by measuring artero-venous differences in blood sugar concentration, and published a series of papers of great theoretical and practical interest. The author found that the A-V difference is always positive, indicating a constant peripheral glucose utilization which increases during postprandial hyperglycemia and decreases in hypoglycemia. The peripheral utilization of glucose thus contributes to the extrahepatic control of glucose homeostasis. Insulin administered with glucose was found to stimulate its utilization, but if hypoglycemia is allowed to set in, the utilization decreases allowing the blood sugar to rise again. According to Somogyi this is due to the stimulation of the pituitary-adrenal secretion by hypoglycemia. This insulin-activated anti-insulin mechanism can overpower insulin, especially in the diabetic patient where insulin hypoglycemia may be followed by hyperglycemic tides with glycosuria and ketonuria, and may lead the unaware physician to increase the dose of insulin and enter into a vicious cycle.[12] The interference of the pituitary-adrenal system with the action of insulin also explains the lack of stoichiometric relationship between dose of insulin and amount of glucose utilized.

A relationship between blood sugar concentration and activity of the pituitary-adrenal system is suggested also by the work of Steeples and Jensen[13] and of Paschkiss and collaborators[14] who,

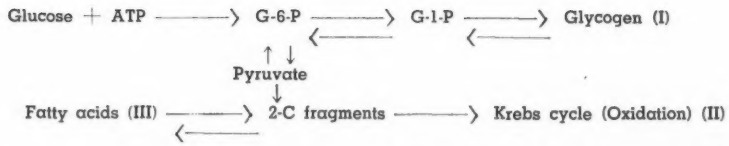
measuring adrenal cholesterol and blood glycogenic corticosteroids, showed that hyperglycemia inhibits and hypoglycemia stimulates the adrenal cortex. Hypoglycemia could thus be considered a form of specific stress. Gordon[15] goes as far as suggesting that any stress may cause a disturbance of protein and carbohydrate metabolism leading to hyperglycemia, the degree of which would depend upon the functional adequacy of the islet tissue in response to the increased load. In individuals with hereditary, congenital or acquired low reserve, a temporary or permanent pancreatic decompensation may occur, and the prophylactic use of insulin may be a wise measure of protection. Gordon's hypothesis is not without some basis in clinical evidence, as Hinklem and collaborators[16] actually demonstrated that stressful life situations may cause a rise in blood glucose and ketone bodies of diabetic patients and attributed the effects observed to a stimulation of the pituitary-adrenal anti-insulin system.

Other aspects of the relationship of the pituitary and the adrenal cortex have been investigated. Wilder[17] studied the nature of the diabetogenic hormone of the anterior pituitary which he considers closely related to the growth hormone. This is in agreement with the observations of DeBodo and collaborators[18] who found that a highly purified growth hormone preparation abolishes the insulin hypersensitivity of hypophysectomized dogs and produces an impairment of the glucose tolerance. Martinetti and Andreani[19] found that alloxan diabetes in rabbits is aggravated by anterior pituitary extracts and Lotspeich[20] found that a purified growth hormone causes a rapidly fatal intensification of glycosuria and ketosis in alloxan diabetic dogs. This severe diabetes is associated with marked destruction of body proteins and increased blood amino acids, an observation which may be of great significance in view of the findings of Conn and collaborators[21]. These authors showed that the injection of 120 to 150 mg. of ACTH daily to 3 normal subjects produced a reversible diabetes with reduced carbohydrate tolerance, glycosuria and negative nitrogen balance. Subsequent experience confirmed the fact that diabetes is a possible complication of prolonged treatment with ACTH. Lotspeich[20] confirmed the diabetogenic action of ACTH showing that it has the same action as the growth hormone on blood amino acids and states that one should not refer to "the" diabetogenic hormone of the anterior pituitary, as there are at least two of them. In view of the fact that cortisone and other adrenal cortical steroids can produce a diabetes-like syndrome (see 22 for references), one wonders if ACTH acts directly or through the adrenal cortex. The growth hormone also may exert its influence through the adrenals: Park and Krahl[23] found that a pituitary factor which follows the growth hormone during fractionation and crystallization depresses the glucose uptake of rat diaphragms to diabetic levels, but is not active in the absence of the adrenal glands.

These important contributions help understand why the maintenance of a normal blood sugar concentration appears to depend upon the balance between anterior pituitary and adrenal cortex on the one hand and pancreas on the other, and why diabetes may arise either following increased activity of the pituitary-adrenal system or following decreased activity of the pancreas. What are the possible mechanisms of the diabetogenic action of the pituitary-adrenal system? Several possibilities have been or can be suggested.

The Hexokinase Enzyme System. The first step in the utilization of glucose is its phosphorylation to glucose-6-phosphate by ATP. This phosphorylation is catalyzed by hexokinase. Some of the glucose-6-phosphate is then converted to glucose-1-phosphate and hence to glycogen, while the rest is degraded to 3-, then to 2-carbon fragments and then either oxidized via the Krebs cycle or utilized for the synthesis of fatty acids.

Thus, there are three main paths of glucose metabolism: glycogen synthesis (I), oxidation to CO_2 and H_2O (II), and conversion to fatty acids (III). All three paths are known to be favored by insulin, a fact which could be explained if one could prove that insulin stimulates



the activity of hexokinase. That this might be the case is suggested by the work of Cori and collaborators.[24-28] These authors found that of all the possible hexokinase present in the rat diaphragm, only 50% is active in the normal animal and only 25% in the diabetic. It rises to 75% following removal of the pituitary and to 100% with further addition of insulin. Cori and collaborators also found that the anterior pituitary and adrenal cortical extracts inhibit the hexokinase reaction *in vivo* and that insulin, although without direct effect on hexokinase, nullifies the pituitary and adrenal inhibition. Thus an excess of pituitary or adrenal cortical activity or a lack of insulin would result in an impairment of hexokinase function and phosphorylation of glucose; hence its utilization would be slowed down. There would be less glycogen and fatty acid synthesis, less glucose oxidation and symptoms of diabetes would appear. On the other hand, hypophysectomy would ameliorate diabetes by removing one of the sources of hexokinase inhibition. Villee and collaborators[29] have presented data in support of Cori's theory. Others (Broh-Kahn and Mirsky[30]) have obtained inconsistent results; still others (Stadie and Hangaard[31]) have been unable to detect any difference between the hexokinase activity of normal and diabetic tissues. The greatest difficulty in accepting hexokinase as the only mediator of insulin action is the well established fact that hypophysectomized and/or adrenalectomized animals are very sensitive to insulin. If insulin were to exert its metabolic effects by nullifying the hexokinase inhibiting action of the pituitary and the adrenal cortex, insulin would be without effect in the absence of these glands, and the hypophysectomized-adrenalectomized animal would be insensitive rather than oversensitive to insulin. To this one must add the observation of Zwilling[32] that insulin hypoglycemia can be obtained in the 5-day-old chick embryo, before differentiated pituitary or adrenal cortical cells have appeared.

Three explanations have been offered for this contradiction: a) that the pituitary and adrenal inhibitors are very labile and difficult to demonstrate[25]; b) that there are other hexokinase inhibitors of unknown origin in muscle[33] or plasma[34]; c) that, in addition to its indirect effect on the hexokinase system, insulin acts directly on other enzymes, possibly in the Krebs cycle[35].

Although strengthened by recent reports indicating similarity between anterior pituitary diabetogenic factor, growth hormone and hexokinase inhibiting factor (see 36 for references), the hexokinase theory cannot be accepted without reservations as yet.

The SH-containing enzymes. Among the enzyme systems which require the -SH group for their activity are those necessary for the synthesis of insulin. Alloxan produces a decrease in blood glutathione concentration. Since alloxan, a highly diabetogenic substance, is similar to uric acid, the suggestion has been made that human diabetes may be the result of a disturbed purine metabolism with production of alloxan-like materials and reduction of the amount of -SH groups available for the synthesis of insulin. This hypothesis has been strengthened by the observations of Houssay[37], Martinez[38], Saliprandi[39], and others that glutathione and other -SH-containing substances (such as cysteine and thiouracyl derivatives) protect the animals from the diabetogenic action of alloxan and by the observation of Griffith[40] that animals on a methionine-cysteine free diet, which reduces the -SH supply, develop diabetes following the administration of normally non-diabetogenic purines. Conn et al.[41] showed that ACTH-induced diabetes is associated with increased uric acid excretion and a fall in blood glutathione and that the injection

of reduced glutathione causes a decrease in blood sugar and an abrupt disappearance of the glycosuria. Finally, Griffith[42] showed that alloxan inhibits the action of muscle hexokinase.

On the basis of these observations, one is tempted to suggest that pituitary or adrenal hyperfunction, perhaps activated by stress, might result in 1) a disturbance of purine metabolism with production of excessive amounts of uric acid and/or alloxan-like materials; 2) a decreased concentration of glutathione in the blood with increased sensitivity of the islet cells to these purines and reduced insulin production; 3) inhibition of the hexokinase activity; and 4) hyperglycemia with increased demand on the beta-cells of the pancreas followed by a pancreatic decompensation and degeneration of the insular tissue[43]. In this manner pituitary or adrenal hyperfunction would contribute to the appearance of diabetic symptoms, hypophysectomy or adrenalectomy to their disappearance.

* * *

Are there pancreatic hormones other than insulin? This is a question suggested by the results reported in a number of recent papers.

The two most common types of experimental diabetes, pancreatic and alloxan diabetes, differ in some essential features. The alloxan diabetic animal has a higher blood sugar, requires more insulin to become aglycosuric, but has little or no tendency to ketosis[44-48]. The removal of the pancreas in the alloxan diabetic animal causes it to become similar to the depancreatized animal: hyperglycemia and insulin requirement decrease and tendency to acidosis increases as if, with the pancreas, the alloxanized animal had been deprived of some factor capable of elevating the blood sugar on the one hand and preventing ketosis on the other[49-54].

The Hyperglycemic Factor. It is known that the intravenous injection of insulin is followed by a short period of hyperglycemia, a phenomenon observed many years ago and attributed to impurities[55-57]. Recently the "impurity" has been isolated from insulin and from pancreatic tissue and called "Hyperglycemic Factor (HGF)" or "Glucago"[58-67]. The HGF produces hyperglycemit by bringing about liver glycogenolysis[68, 69] and is active in normal and diabetic animals but not in animals with severe diabetic ketosis (presumably because these animals have little or no liver glycogen[70, 71]). The HGF can be demonstrated *in vivo* by anastomosing the pancreatic vein of an alloxan-diabetic animal with the femoral vein of a normal one[72]; it can be isolated from the beta-cell-free pancreas of alloxan treated dogs and from the pancreas after ligation of the ducts and degeneration of the acinar tissue. For these reasons it has been called the "alpha-cell hormone."

The secretion of HGF by the alloxanized pancreas can explain the marked hyperglycemia of alloxan-diabetic dogs, but does not explain the absence of ketosis in these animals. Possibly alloxan-diabetic animals do not develop ketosis because their liver contains more glycogen and preserves it more tenaciously in fasting than do normal animals[73], or perhaps because carbohydrate oxidation does not appear to be impaired in alloxan-diabetic tissues as in the tissues of depancreatized animals[6-8]. These findings, although adequate to explain the lack of ketosis in alloxan diabetes, do not rule out the interesting possibility that the pancreas of alloxan-treated animals may secrete an antiketosis principle, a possibility which was investigated[74-75]. Crude insulin-free extracts from pancreas of alloxan-diabetic dogs, normal dogs and normal hogs were prepared and injected intravenously into dogs with ketosis due to fasting, to alloxan or to pancreatic diabetes. Following the injection of the extracts (which contained the hyperglycemic factors), the blood sugar rose while the concentration of the ketone bodies in the blood decreased markedly. It is well known that an increased availability of carbohydrate to the liver can, in itself, lower the blood ketones. This happens, for instance, in hyperglycemia following administration of glucose. It was, therefore, necessary to rule out the possibility that the observed decrease in ketone bodies was due to the simultaneous increase in blood sugar. Hyperglycemia was therefore produced by injecting a

purified hyperglycemic factor* as well as by injecting epinephrine. In both cases a marked hyperglycemia was produced, but the concentration of ketone bodies increased instead of decreasing. This is not surprising, as both epinephrine and the HGF induce hyperglycemia by stimulating liver glycogenotysis and result in a decrease in the amount of carbohydrate available to the liver. Since the pancreatic extracts used in our experiments contained the hyperglycemic factor, one could say that they produced a lowering of the ketone bodies concentration in the blood despite the associated hyperglycemia, rather than because of it. Experiments are in progress to study the nature of this phenomenon.

Future work might prove that the pancreas, like the pituitary or the adrenal cortex, is not a single-hormone gland, but secretes not only insulin (hormone of the beta-cells), and the hyperglycemic factor (hormone of the alpha-cell[76]) but, perhaps, a substance concerned with lipid metabolism (lipocaic[77, 78]) and one concerned with the regulation of ketone bodies metabolism.

REFERENCES.

1. Bondy, P. K., J. Clin. Invest., **27**, 526 (P), 1948.
2. Bondy, P. K., James, D. F., and Farrar, B. W., J. Clin. Invest., **28**, 238, 1949.
3. Bondy, P. K., Bloom, W. L., Whitner, V. S. and Farrar, B. W., J. Clin. Invest. **28**, 1126, 1949.
4. Lipscomb, A., and Crandall, L. A., Jr., Amer. J. Physiol., **148**, 303, 1946.
5. Crandall. L. A., Jr., and Lipscomb, A., Amer. J. Physiol., **148**, 313, 1946.
6. Zilversmit, D. B., Chaikoff, I. L., Feller, D. D., and Masoro, E. J., J. Biol. Chem., **176**, 389. 1948.
7. Feller, D. D., Strisower, E. H., and Chaikoff, I. L., J. Biol. Chem., **187**, 571, 1950.
8. Feller, D. D., Chaikoff, I. L., Strisower, E. H., and Searle, G. L., J. Biol. Chem., **188**, 865, 1951.
9. Chaikoff, I. L., Lerner, S. R., Enterman, C., and Dauben, S. G., J. Biol. Chem., **174**, 1045, 1948.
10. Weinhouse, S., Millington, R. H., and Friedman, B., J. Biol. Chem., **181**, 489, 1949.
11. Somogyi, M.,—a. J. Biol. Chem., **174**, 189, 1948.
    b. Ibid. 597.
    c. Ibid., **179**, 217, 1949.
    d. Ibid., 1289.
    e. Ibid, **186**, 513, 1950.
12. Somogyi, M., 116th Meet. A. C. S. Atlantic City, Sept., 1949.
13. Steeples, G. L. and Jensen, H., Am. J. Physiol., **157**, 418, 1949.
14. Paschkis, K. E., Cantarow, A., and Boyler, D., Fed. Proc., **8**, 123, 1949.
15. Gordon. E. S., in Pituitary-Adrenal Function. A.A.A.S. Symposium 1950, 193.
16. Hinklem, L. E., Jr., Conger, G. B., and Wolf, S., J. Clin. Invest., **29**, 754, 1950.
17. Wilder, J., A. J. Dig. Dis., **15**, 183, 1948.
18. De Bodo, R. C., Kurts, M., Ancowitz, A., and Kraig, S. P., Proc. Soc. Exp. Biol. and Med., **74**, 524, 1950.
19. Martinetti, R., and Andreani, G., Boll. Soc. It. Biol. Sper., 1949, **25**, 744.
20. Lotspeich, W. D., J. Biol. Chem., **185**, 221, 1950.
21. Conn, J. W., Louis, L. H., and Wheeler, C. E., J. Lab. and Clin. Med., **33**, 651, 1948.
22. Ingle, D. J., A Review, J. Clin. Endocr., **10**, 1312, 1950.
23. Park, C. R., and Krall, M. E., J. Biol. Chem., **181**, 247, 1949.
24. Price, W. H., Cori, C. F., and Colowick, S. P., J. Biol. Chem., **160**, 633, 1945.
25. Colowick, S. P., Cori, G. T., and Stein, M. W., J. Biol. Chem., **168**, 583, 1947.
26. Krahl, M. E., and Cori, C. F., J. Biol. Chem., **170**, 607, 1947.
27. Krahl, M. E., and Park, C. R., J. Biol. Chem., **174**, 939, 1948.
28. Stein, M. W., Cori, G. T., and Cori, C. F., J. Biol. Chem., **186**, 763, 1950.
29. Villee, C. A., Sinex, F. M., and Solomon, A. K., Feder. Proc., **7**, 197, 1948.
30. Broh-Kahn, R. H., and Mirsky, J. A., Science, **106**, 148, 1947.
31. Stadie, W. C., and Haugaard, N., J. Biol. Chem., **177**, 311, 1949.
32. Zwilling, E., Proc. Soc. Exp. Biol. and Med., **67**, 192, 1948.
33. Perlmutter, M., and Greep, R. O., J. Biol. Chem., **174**, 915, 1948.
34. Christensen, W. R., Plimpton, C. H., and Ball, E. G. J. Biol. Chem., **180**, 791, 1949.
35. Cori, C. F., The Harvey Lectures, **41**, 253, 1945-46.
36. Beaser, S. B., New England J. Med. **243**, 81, 133, 1950.
37. Houssay, B. A., and Martinez, C., Rev. Soc. Argentina Biol., **24**, 123, 1948.
38. Martinez, C., Ibid. **64**, 127, 1950.
39. Saliprandi, N., and Saliprandi, D., Boll. Soc. Ital. Biol. Sper., **24**, 1, 1948.
40. Griffiths, M., J. Biol. Chem., **184**, 289, 1940.
41. Conn, J. W., Louis, L. N., and Johnston, M., Science, **109**, 279, 1949.
42. Griffiths, M., Arch. Biochem., **20**, 451, 1949.
43. Lukens, F. D. W., Proc. Am. Diabetes Assn., **10**, 103, 1940.
44. Dragstedt, L. R., Allen, J. G., and Smith, E. M., Proc. Soc. Exp. Biol. and Med., **54**, 292, 1943.
45. Goldner, M. G., Clark, D. E., J. Clin. Endocr., **4**, 194, 1944.
46. Fallen, L. S., and Szilagyi, D. E., Ann. Surg., **128**, 639, 1948.
47. Gaston, E. A., New England J. Med., **238**, 345, 1948.
48. Banergie, S., and Gangagobinda, B., J. Biol. Chem., **178**, 145, 1949.
49. Thorogood, E., and Zimmermann, B., Endocr., **37**, 191, 1945.
50. Candela, J. L. R., Rev. Clin. Espanola, **19**, 393, 1945.
51. Candela, J. L. R., Goni, P. M., Caldeiro, M. R., and Carreras, P. G., Trav. Inst. Nac. Ciencias Med. Madrid, **9**, 89, 1947.
52. Cavallero, C., and Malandra, B., Boll. Soc. It. Biol. Sper., **25**, 85, 1949.
53. Cavallero, C., and Mallandra, B., Bol. Soc. It. Biol. Sper., **25**, 87, 1949.
54. Ingle, D. J. and Nezamis, J. E., Proc. Soc. Exper. Biol. and Med., **71**, 315, 1949.
55. Fisher, W. F., Amer. J. Physiol., **67**, 57, 1923.
56. Murlin, J. R., Clough, H. D., Gibbs, C. B. F., and Stokes, A. M., J. Biol. Chem., **56**, 253, 1923.
57. Bellido, J. M., Arch. Intern. Pharmacodyn et Ther., **38**, 456, 1930.
58. Heard, R. D. H., Lozinski, E., Stewart, L., and Stewart, R. D., J. Biol. Chem., **172**, 856, 1948.
59. Zimmermann, B., and Donovan, T. J., Amer. J. Physiol., **153**, 197, 1948.
60. Sutherland, E. W., and DeDuve, C., J. Biol. Chem., **175**, 663, 1948.
61. Pincus, G. J., Kamarov, S. A., Snape, W. J., and Shay, H., Amer. J. Physiol., **155**, 460, 1948.
62. Sutherland, E. W., Cori, C. F., Haynes, R., and Olsen, N. S., J. Biol. Chem., **180**, 825, 1949.
63. Gaede, K., Ferner, H., and Kastrup, H., Klin, Wschr., **28**, 388, 1950.

(Continued on page 32)

***The Hyperglycemic Factor used in these experiments and the Insulin used for the maintenance of our depancreatized dogs were generous gifts of Eli Lilly and Company.**

PSYCHOSOMATIC CONCEPTS

By

H. H. GARNER, M. D.*

The "cause" in illness is being replaced by the concept of causative factors. Causative factors have been described under the three categories of predisposing, provoking and perpetuating agents. These influences are invariably present in the causation of all illness. The importance of environmental and social factors as causative agents needs to be emphasized in the understanding of illness. Impacts by the environment may be sudden or insidious, massive or minimal. The concept of specific disease entities comes closest to realization in the infectious diseases caused by specifically identifiable organisms, and almost has no place in many of the degenerative conditions. Even in such "specific" entities as tuberculosis, there are many causative factors which act as predisposing, provoking and perpetuating agents.

Health too, is an abstraction. The degree of health may be said to parallel effectiveness in living, and disease as inducing ineffectiveness in the somatic and psychic activities of the individual. Disease, likewise, mobilizes the adaptive resources of the individual. The adaptive responses to stress are among the most important physiological reactions in life and the capacity to adjust to external stimuli among the most characteristic features of living matter. Stress, it must be emphasized, includes not only such external dangers as are apparent in agents destructive to tissue and agents which invade the organism. It also includes the types of stress which are an expression of the frustrations created by goal directed and motivationally induced behavior brought about by the needs of the organism (food, shelter, clothing, sexual satisfaction, etc.) when such behavior does not lead to satisfaction.

"Man is the core of medicine. Visualizing individual man in relation to the cosmos, we see on the one hand that he is composed of myriads of minute cells and microscopic structures operating in health as a highly integrated, harmonious, cooperative cellular biochemical organism. On the other hand, man, when multiplied many-fold, becomes society. The whole, however, is more than the sum of its parts. As man is composed of cells, so society is composed of men. Man, the individual, lives in two concomitant environments. Both are complex. The tissues and chemical reactions and the equilibria of the organism constitute the realm of the biological sciences; the social and external environment is the realm of social medicine. Clinical medicine, between these two, is concerned with the indivisible individual. Psyche and soma, internal homeostasis, growth, and atrophy and adaptation to external environmental forces are all part of the domain of clinical medicine. Looking at man with the naked eye he is an individual. Studying man with microscopes, both visual and electronic, he is biological. Stepping back and viewing man through a telescope, he becomes a small unit of society. All three perspectives are requisite to full comprehension." The above quotation from Stieglitz very aptly describes the psychosomatic concept.

Probably no one knew as much about psychosomatic medicine as the general practitioner prior to the period of emphasis on specialty education. Specialty practice was an outgrowth of the scientific developments which followed the period of emphasis on pathology and organ changes which had its stimulus in the studies of Virchow in Vienna. This emphasis on understanding the diseases of the specific organ or organs within the realm of the particular specialist's functions was the natural outgrowth of the period. Psychiatry, too, was dominated by this influence and attempted an understanding of mental illness in relation to the pathologic or physiologic changes which could be demonstrated as being present for certain supposed disease en-

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tities. Such emphasis was responsible for many advances in the mechanistic understanding of illness, but the trend in recent years is swinging toward an understanding of the individual as a whole operating in a certain environmental setting.

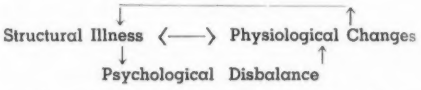
Modern psychiatry has been striving for a dynamic understanding of the individual and the symptoms he has, as against being concerned with the symptoms and their classification. To understand the patient we consider it necessary to study not only the symptoms but the individual in his physical, mental and emotional totality. Likewise, we must study the individual in his social, economic and cultural surroundings. The psychosomatic approach to the study of illness is essentially that expressed in the concept of a dynamic rather than a mechanistic and descriptive view of psychiatry.

Essentially what is being said is that psychosomatic medicine is not a specialty but a concept of illness in which all manifestations of bodily disturbance can be looked upon as expressing a breakdown in the homeostatic balance of the patient. The breakdown affects the individual as a whole physiologically, psychologically and structurally in varying degrees of intensity. Mental and physical symptoms are present in any homeostatic disbalance, and express utilization of earlier adaptive patterns of meeting stress, loss of function, irritative symptoms and attempts at restitution. The predominant group of symptoms seen tends to lead the clinician to classify the illness as:

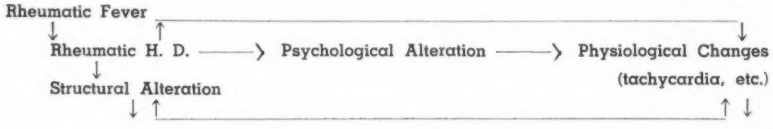
1. Structural
2. Physiological or biochemical
3. Psychological or functional

1. *Patient with Structural Changes*

Structural illness is hardly an expression with which you are likely not to be familiar, but frequently the importance of the psychological and physiologic concomitants receive less attention than they merit. Seldom, if ever, is it possible to consider structural (organic) illness other than as expressed in the following formula; that is, an expression of illness which is almost always interrelated with and influenced by the physiological and psychological alteration.



There is little need to dig deeply to discover examples of structural illness to which this formula is appropriate. In the field of cardiovascular diseases one is frequently able to elicit histories which read somewhat as follows: The patient may have developed a rheumatic heart disease rather early in life. The mother, possibly because of guilt feelings concerning her care and attitude toward the child and feeling that somehow she may have been responsible for the illness, makes the child very dependent and excessively fearful of possible physical results. The physician may likewise add to the noxious influences. Statements which may seem innocent may be exceedingly traumatic because of the significance of authority to the patient. The patient at some later date may exhibit extreme cardiac disability whenever he is consciously threatened with being abandoned by the mother or a mother substitute, or in circumstances which in some manner express a threat to physical well being. This may be expressed as:



2. *Physiological Alteration, as Illness*

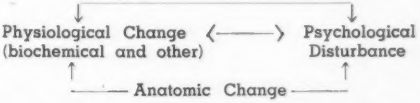
Patients are frequently seen who show rather marked evidence of physiological disturbance and are considered as having a disease, the nature of which is a dysfunction in the autonomic nervous system. A classical example of such a physiological disturbance was the condi-

tion diagnosed as neurocirculatory asthenia in the first world war, but recognized and understood by most physicians today as an expression of anxiety in which the most overt manifestation is in cardiorespiratory symptoms. Many of the cardiac dysrhythmias are evidence of disturbed psychological functioning. An example of such a case, in which there was severe cardiac disability with tachycardia as the outstanding symptom, is the following:

The patient was a 40 year old woman who during her pregnancy visited a race track, accidentally stumbled and was slightly injured. She delivered at term a child with a congenital heart defect. Guilt feelings on the part of the mother led to the development of a highly protective environment for the child with extreme maternal dependence being shown by the child and identification of the mother with her child. Although quite concerned about the advisability of a long railroad journey, the mother nevertheless decided to take the child on a trip. While traveling, the child became ill and within a short time died. Cardiac symptoms in the patient appeared soon afterwards and were completely incapacitating. The formula for clinical manifestations of disease reads:

Psychological Stress (injury at race track) ⟶ Guilt Feelings (a form of anxiety) ⟶ Physiological Changes (tachycardia, etc.)

Physiological expression of illness also occurs in a manner more directly related to biochemical alteration than to psychological influences. In illnesses affecting the chemical mediators at the neuromuscular junction, we see such classical examples as myasthenia gravis and myotonia congenita. In such illness biochemical alterations apparently express changes in biochemistry in which no obvious anatomic or psychologic change precedes the development of the biochemical dysfunction. However, anatomic and psychologic dysfunction may follow the biochemical disturbance.



3. *Psychological Dysfunction Leading to Structural (Organic) Change*

There is usually some difficulty in comprehending the relationship between psychological factors and their influence in producing structural change. A digression for a moment may help to clarify this relationship. There are several levels of functioning in the central nervous system when studied in terms of degree of awareness by the individual of the stimulus producing behavior or physiological changes.

Some functions are carried out at a level in which patterns of behavior may be considered as being fixed in the tissues of the organism. A typical example of such activity which may be carried out without awareness is the reflex response to tendon stimulation. In these responses the adaptive changes to environmental stimuli are channelized and fixed. They do not require any experiential phenomena for development and maturation.

Conscious responses are those in which the perceptive, integrative and expressive components of an adaptive response are within the awareness of the individual. The awareness of danger or some threat may lead to anxiety, rage or dependent longing which is consciously appreciated by the organism. In a formula this would read about as follows:

Stimulus ⟶ Fear ⟶ Physiological Reaction { Activity (Neuro-muscular, mental activity, expressive behavior, somatic expression)

Unconscious processes are more productive of physiological changes than is generally appreciated and it is through the chronic physiological changes, which appear as a result of inability of the or-

ganism to express at the highest possible levels of the nervous system the emotional responses of the individual, that structural alteration may occur. Emotions are accompanied by physiological concomitants appropriate to the needs of the organism for such an emotional response. The physiological changes appear as alterations in the organs supplied by the autonomic nervous system, the motor apparatus, the peripheral sensory system and the organs of perception. The role of the unconscious, as used psychiatrically, in the development of somatic changes as a result of psychological disturbances, cannot be completely elucidated at this time. I would prefer to give a short clinical case history to point out the influence of psychological determinants in the production of permanent structural change.

An 18 year old well-built negro boy came to Chicago from Alabama three years prior to his being seen in the hospital clinic. He came from a family in which the maternal and paternal influences were considerable in molding the three brothers to follow a pattern of ingratiating, passive, non-offensive behavior to the white neighbors. There was never any question of "his place" in the society. On coming to Chicago he found himself a very well accepted student and athlete in his high school and was offered a position as class officer at graduation which he rejected. He was always in good physical health and had been found to be so on examination for the basketball team. On leaving school he anticipated getting a position above that of a laborer, and attempted to deny to himself that he would be unacceptable to potential employers. His first experience was one of being told that no position was available, although two white boys alongside the patient were hired. He immediately denied any anger at having been so humiliated but later admitted he was intensely angry. At the next two jobs he was refused because of a finding of hypertension on physical examination. The anticipation of future rejections had so mobilized his anger that the cardiovascular system reacted as if the patient were in a stage of continued rage with no outlet of tension in neuromuscular, verbal or other channels of expression that are said to be associated with hypertension, with resulting morphologic changes when the physiologic state has become chronic.

Psychological disturbance leads to structural change when a situation causing conflict is present and expression cannot occur through and be drained by discharge, e.g. action, thoughts or words, or expressive behavior such as laughing or crying. The energy drains into the vegetative nervous system or neuromuscular system. Frequently the responses occur in the autonomic nervous system or the neuromuscular system, whichever is the appropriate channel of expression of the emotion being contained. When such an exaggerated activity is maintained in the autonomic nervous system the changes produced by chronicity may lead to structural alteration. This may be expressed in a formula as follows:

Psychological Stress —〉 Physiological Changes (chronic) —〉 Structural Alteration

The energy is expended in changes which are inappropriate for adequate solution and working through of the problem.

Specificity of Somatic Response (Choice of Organ)

The question of specificity of the somatic expression of disturbed psychological function is an unsettled problem. Alexander has indicated that physiological responses to emotional stimuli vary according to the nature of the precipitating emotional status. For instance, laughter expresses merriment; likewise each emotional state has its own physiological syndrome, such as the syndrome of blood pressure elevation and accelerated heart beat with rage. Two chief modes of preparation for dealing with anxiety-producing situations is suggested: that of meeting it actively, which mobilizes the sympathetico-adrenal system, and that of retreating to a state of increased dependence and help-seeking in dealing with the emergency. This

mode of preparation is associated with mobilization of the parasympathetic system. French suggested that "symptoms resulting from the frustration of an activity are likely to involve especially the organs which are most active or under most tension at a moment of frustration." For instance, the displacement of energy from an inhibition of a neuromuscular response by frustrating circumstances might lead to an intensification of activity in intellectual processes, in which case the symptoms would appear in the organ under most tension during the frustration, the brain, and the symptom would be headache. There are other aspects of the specificity of somatic expression when there is a disturbance in psychological functioning not clearly indicated in the literature. The following factors are suggested as some of the determinants of the specificity of the somatic reaction with disturbances in psychological function.

Conversion Phenomena

Somatic expression, the symptoms which the patient finds subjectively uncomfortable and may be observed clinically are said to be a symbolic expression of an emotionally charged psychological tension. This expression takes place in the voluntary neuromuscular and in the sensory perceptive systems. The conversion phenomena are adaptive either as:

(1) A means of substitutively inhibiting a function (usually sexual), e.g. paralysis of an extremity prevents the masturbating activity and also prevents the occurrence of an erection. The extremity is inhibited from acting, acts like, and acts as a substitute for a nonerect genital.

(2) The conversion phenomena may have the adaptive value of expressing through a substitutive organ or organs that which the patient is fearful of having expressed by the organ itself. An example of such phenomena is seen in pseudocyesis, where the rectum acts like a retaining organ. The gastrointestinal tract is substituted for the uterus and feces are retained.

Organ Neuroses

This term has been used to denote those disturbances in function in which the symptoms subjectively noted and clinically observed express the physiological reaction to an emotional state. The physiological expression is inappropriate because it appears in response to unconscious motivating psychological content and does not resolve the conflict. The classical example of such responses is that of hypertensive reaction and the concomitant subjective and observable reactions to rage. The responses are appropriate to a situation which calls forth an active overcoming of an aggressive force, but have little utility in dealing with the problems of hostility provoked by unconscious factors and for which the adequate discharge is not possible through neuromuscular or expressive channels. The symptoms found in many of the organ neuroses will, like the symptoms of conversion hysteria, express:

(1) Activation of certain bodily structures, e.g. cardiovascular, producing hypertension and tachycardia.

(2) Inhibition of other structures, e.g., weakness of the body experienced subjectively and sometimes clinically. This adaptive response of weakness prevents the carrying out of a neuromuscular act, striking the individual toward whom the rage is directed.

Symptoms of Expressive Innervation

Such physiological processes as crying, laughing, blushing, grimacing, gesticulating are rather complex responses in which a more or less specific emotional feeling is associated with certain specific physiological reactions, i.e. crying is associated with loss of love, laughter with amusement. Again, as with other types of symptoms, one may find:

(1) The physiological expression is appropriate for and is a means of actively expressing a feeling tone.

(2) It may have the adaptive significance of inhibiting the expression of feelings which require repression or suppression and also be a substitute for the

emotional feeling tone which must be inhibited. Laughing may be a means of inhibiting and a substitution for crying. Blushing inhibits and substitutes for desires to exhibit.

Localized and Limited Types of Organ Reaction

Many symptoms seem to express localized somatic and physiological reactions. They do not express the substitution for and acting like another organ as is the case in conversion symptoms. They likewise do not represent innervations of the sympathetic or parasympathetic systems as specific emotional responses appropriate to the affect being expressed, e.g. tachycardia, hypertensive reaction, peripheral vasoconstriction with anger. These symptoms seem to have a rather complex basis for the "choice of organ." Among the factors involved in the choice of organ are regression, identification, and introjection, the elucidation of which is not possible in this paper. Something might also be said for the concept that that organ is involved which is under most tension during frustration. Some general statements which might explain this group of localized symptoms follow. The symptoms are usually, if not always, a response to the unconscious phantasy produced by some situation, event, stimulus or other initiating influence. The symptoms express:

(1) The physiological reaction to the phantasied organic alteration, e.g. the phantasy which carries with it the meaning "I have gonorrhea," which is not uncommonly seen as a reaction to the guilt of extramarital relations, produces increased frequency, urgency, tenesmus and burning on urination. The organ physiologically reacts as if infection were present.

(2) Those physiological changes which represent attempts at inhibition of the noxious effects of the phantasied somatic alteration or attempts at healing. A patient who phantasied arthritic changes in the shoulder joint developed a splinting of the joint through neuromuscular responses which might very well represent the attempts at inhibiting joint activity (healing).

(3) Symptoms which are similar to those of other individuals, the mechanisms of identification and introjection contributing to the physiological alteration. Choking sensations in a patient whose father died of a carcinoma of the lung after a period of prolonged difficulty with respiration is offered as an example.

There have been several basic elements indicated as operative in the choice of organ for expression of the tension which cannot be drained off by or through motor activity, expressive innervations and mental activity. For any patient at any time, all of these modes of organ expression may be operative at once. The symptoms represent the total of all physiological and structural change produced by the response of an individual to any stimulus, situation or event when effective responses through the neuromuscular, expressive, and psychic apparatus are blocked. The responses are adaptive in nature but they are erratic, lacking in utilitarian value, uneconomical. They do, however, have defensive value and tend to prevent a more severe disintegration of total functioning.

Summary

When the individual is faced with circumstances which provoke feelings of love, anxiety, anger, shame, guilt or dependent longing, there is a response which is motivated by the needs of the organism and is goal directed. The behavior is in the nature of activity directed at seeking satisfaction or at creating changes in the individual or his surroundings to decrease unpleasantness. The responses are expressed in thoughts or words, actions, or expressive behavior such as crying and laughing. Such behavior tends to drain off energy and restore the psychological homeostasis of the individual. When feelings are blocked so that expression cannot occur through these suitable channels, the discharge of energy takes place into the soma leading to symptoms resulting from physiological and later morphological alteration. Not only does the body react to conscious

and unconscious feeling appropriate to the stimulus of all external and internal influences operative at any particular time, but also to the feeling tones and somatic changes appropriate for the unconscious and conscious phantasies being mobilized. The symptoms likewise represent the totality of all the organ reactions to the actual and phantasied situations taking place at any particular time and include symptoms which represent the active response to the stimuli, inhibition of response and those which represent attempts at restitution. It is seldom, if ever, that only one particular system response, e.g. sympathetic system response, can explain the totality of all the organ expressions in any patient at any one time.

In the evaluation of the patient who comes to the physician for care, it would seem that attempts to understand the patient must be made with certain goals in mind. These goals are the alleviation of the patient's distress and the reestablishment of a degree of health which will enable the patient to make full use of his resources in living a life with sufficient satisfactions and economy of effort so that his relationship with society is one which leads to a constructive use of his resources. To achieve these goals one must be aware of the motivating factors which bring the patient to the particular physician at the time he chooses for his visit; the goals of the individual and how he expects to fulfill his needs by visiting the physician; the environmental influences on the patient and how they have modified the patient's behavior; the stresses in the life of the individual which have created behavioral tendencies which are lacking in economy, are vacillating, erratic and substitutive.

REFERENCES

1. Alexander, F. & French T. Studies in Psychosomatic Medicine, The Ronald Press, New York, 1948.
2. Alexander, Franz. Psychosomatic Medicine, W. W. Norton & Co., New York, 1950.
3. Dunbar, Flanders. Emotions and Bodily Change, Columbia University Press, New York.
4. Fenichel, Otto. Psychoanalytic Theory of the Neuroses. W. W. Norton and Company, New York.
5. Garner, H. H. Genesis of Abnormal Behavior. To be published in the Chicago Medical Schooi Quarterly.
6. Grinker, Roy. Brief Psychotherapy in Psychosomatic Problems. Psychosomatic Medicine. Vol. IX, No. 2. April, 1947.
7. Grinker, Roy. Psychosomatic Medicine, Mental Health Bulletin, I.S.M.H. April, 1948.
8. Masserman. Jules. Behavior and Neuroses. University of Chicago Press, 1943.
9. Selye, Hans. The General Adaptation Syndrome and the Disease of Adaptation. Pharos of Alpha Omega Alpha, December 1947.
10. Stieglitz, Edward. The Integration of Social and Clinical Medicine. Given before the New York Academy of Medicine, March 19, 1947.

A RARE FACIAL MALFORMATION OF A HUMAN FETUS

J. M. ESSENBERG, Ph.D.* and MORRIS GOLDENBERG, M.D.**

A valuable anomaly has been secured by the junior author and added to the embryological collection of The Chicago Medical School. The importance of this specimen depends on the attachment of the placenta to the head of the fetus and the light it sheds on the interpretation of such malformations.

The sitting (CR) height of the male fetus is 35 cm. which places it within the limits of full term intrauterine development. Except for the severe interruption in the formation of the head and the face, and the toes and fingers, to be described presently, the body of the fetus is otherwise normal. The trunk of the body and the extremities are well proportioned and well formed; the skin is smooth and delicate, Fig. 1.

The placenta, being normal in size and structure, is attached to the right side of the lower forehead by means of the amnion and the decidua parietalis. The upper jaw, i.e., the maxillary processes have failed to fuse. Instead the parts have grown towards the attachment of the placenta. The maxillary processes are much longer, thicker and coarser than they are in the normal fetus. The palate, however, has formed and consists of both the hard and soft parts. The uvula, the tongue, the lower jaw, the lower lip and the chin are, to all appearance, normal in development.

Severe interference with developmental processes has occurred in the formation of the nose, upper lip and the eyes. Only remnants of those structures can be found. It seems that the same force that carried the maxillary processes upward prevented the formation of the nose and the upper lip and carried the remnants of those parts towards the attachment of the placenta to the head of the fetus. The upper lip extends the distance of the maxillary processes on both sides, and is separated from the latter by the vestibule. The vestiges of the nose are found on the right side of the face above the remains of the right eye. The opening, Fig. 1, resembling an eye, is in reality the external opening of the nose, inside of which the turbinates of the nose can be identified. The eyes on both sides are represented only by the eyelids; the eyeballs are lacking. The slit between the eyelids is longer on the right side than on the left. The left eye is more in the normal position whereas the right eye is considerably more lateral and lower than the left one. The ears, at least externally, show no marked deviation from the normal except in position; the right auricula is decidedly lower in position than the left one.

The upper part of the head is severely damaged. The brain has failed to form and the meninges, filled with fluid, project out in the form of a crown. The parietal and the greater part of the frontal bones of the skull are lacking. The axial and the appendicular skeletons, except those of some of the digits, appear to be normal in development.

Many of the digits of the hands and feet have either failed to form or have been amputated by bands or strings, presumably amnionic, which are still attached to the damaged surfaces. On the right hand, fingers 1 and 5 are normal, 2, 3 and 4 are amputated and fused. On the left hand, fingers 1 and 2 are normal, whereas 3, 4 and 5 are amputated. On the right foot, toes 1, 2, 3 and 4 are amputated and fused; the fifth toe is normal. All of the toes of the left foot are normal. Figs. 2 and 3.

The report of the junior author, who performed the autopsy, is to the effect that no appreciable malformation of the internal organs was noted. The same applies to the genital organs. The inquiry as to developmental anomalies of the family stock brought negative results.

The name of this kind of anomaly presents certain difficulties. Members of the older school of embryologists classified malformations according to the part of the body involved. The malformation of the trunk was designated as teratocormus; those of the extremities as tera-

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tomelus; those of the head as teratocephalus and those of the face as teratoprosopus. These generic names were then subdivided into specific terms applying to an organ or parts of an organ. If this classification be applied to the present anomaly, the name would be Schistoprosopus anencephalus, which means a fetus with a split face and lack of brain. The above classification presents certain shortcomings and therefore is not widely accepted by students of teratology. However, we have not developed a system of nomenclature that is more exact and enjoys greater popularity.

More obstacles are encountered when the etiology of the present anomaly is considered. There has been a tendency in recent years to consider practically all malformations of genetic origin. Streeter has made a careful study of anomalies in which the amnion is involved. He is convinced that amnionic involvements or amnionic bands, as they are called, are secondary manifestations, in which the primary cause is a defective ovum. That does not, however, mean that the malformation of the face and the head is caused directly by a bad ovum. It is evident that the anomalies are produced by mechanical factors. The stress of the placental attachment has interfered with the hereditary factors of head and facial formation and caused the maxillary processes, the upper lip and the nose to grow upwards and to the right in the line of stress caused by the placenta. The lack of the eyeballs is probably due to pressure atrophy. The lack of part of the fingers and toes would be interpreted by Streeter as a lack of hereditary potentials for those parts, i.e., the seemingly amputated parts did not form at all. The same phenomenon would be interpreted as amnionic band amputations by Winkel, Schwalbe, Edgar and others.

The interpretation that Streeter places upon the defective ovum is that it is

responsible for the initial contact of the amnion with the prospective head region while in the embryonic disc stage of development. The amnion takes its origin partly, if not wholly, from cells of the embryonic disc. This explains why lack of separation may occur in defective ova. However, we do not have sufficient evidence that all amnionic adhesions are caused by bad ova. It is conceivable that mechanical factors of some sort may cause lack of separation or secondary adhesions of the amnion to the body of the embryo. The well-formed and well-proportioned body of this present specimen, the delicate and smooth skin and the lack of congenital anomalies in the family stock lend support to the theory that environmental rather than hereditary factors may be responsible for the production of this anomaly.

LITERATURE CITED

Edgar, James Clifton. 1911. The Practice of Obstetrics. The Blakiston Company.

Schwalbe, E., 1906. Die Morphologie der Missbildungen des Menschen und der Tiere. Part I, pp. 192-202.

Streeter, George L., 1930. Focal Deficiencies in Fetal Tissues and Their Relations to Intrauterine Amputations Contrib. Embryol., **22**: 1-44.

Winkel, F., 1904. Uber Menschliche Missbildungen-Sammlung Klinischer Fortrage v. Volkmann, neue Folge. Gynekologie No. 137.

POST-PARTUM DEVELOPMENT OF BEHAVIOR*

AUSTIN H. RIESEN, Ph.D.**

The title announced for this third lecture of the Series could imply development over a very long age period. Actually, I shall summarize findings and discuss implications of behavior studies covering only the first year or two of the primate life span. The chimpanzee studies to which I shall refer were begun in 1939 under the direction of Dr. Henry W. Nissen at the Yerkes Laboratories of Primate Biology, Orange Park, Florida. The commencement at that time of a program calling for the separation of newborn infants from their mothers, the infants to be reared by hand in a nursery, made possible the study of an age period which was otherwise to a large extent hidden from scrutiny, due to the possessiveness of the mother chimpanzee. Success of the Infant Studies Program, supported in part by the Samuel S. Fels Fund, rested on the background of experience accumulated by Professor Robert M. Yerkes and his associates since about 1925.[24]

The more general implications of this study are derived in part from comparisons between the behavior development of animals at different levels of the phylogenetic scale, particularly between chimpanzee and man. Therefore, I should like to point at the outset to certain indices of growth rate in the chimpanzee. Length of gestation averages 227 days, or about eight tenths as long as in man.[13] Average age at menarche is seven tenths, and average ages of eruption of deciduous teeth and also the appearance of centers of ossification are between five and six tenths of the corresponding ages for man.[11, 12] General body postures which first make their appearance in the behavior of either species during the year following birth show, on the average, a ratio of seven to ten in the ages at which half of the group under observation (Gesell's *critical age*) first achieves comparable behavior items.[18] All of these ratios cited are based on age as measured from the time of fertilization, rather than from date of birth.

From the study of postural development employing the Gesell and Thompson Behavior Examination clear evidence for the dependence of function upon gross structural characteristics is obtained. For example, whereas the human infant "sits unsupported" at 23 weeks of age, and the chimpanzee at 24, corresponding critical ages for raising the head from prone are 27 and 10 weeks, these ages all being reckoned from birth. The first example is rather unusual in that postural items for the chimpanzee only rarely show a critical age later than that for the human. It reflects at least two structural differences between the species: the broader base of support of the human in the sitting position and the longer arms of the chimpanzee which are consequently less readily dispensed with as a means of auxiliary support. The much earlier raising of the head by the chimpanzee is a function of the relatively smaller size and weight of the head, and the shorter neck of the animal.

These two examples illustrate a certain class of genetically determined variables which play a role in determining the sequence of behavioral development, namely, the skeletal proportions of a given species. Evidence that innate neuromuscular factors are also correlated with peculiarities of behavior development is derived from several sources of comparison, both between species and within species.

A first set of comparisons is that which shows that each species of primate develops certain behavior patterns at a stage of growth peculiar to that species. For example, the approximate median age for "rolls to prone" is 40 weeks after birth in the human infant, 11 weeks in the chimpanzee, and in the monkey (*M. rhesus*) this behavior is usually observable on the day of birth. For "bipedal standing" the median ages are approxi-

* Lecture given Feb. 1, 1950, at The Chicago Medical School. This is the third in a series of articles on "The Development of Behavior."

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mately 54 weeks, 39 weeks, and 10 weeks. The last figure, for the rhesus monkey, is based on only that portion of the infant monkey population (about half) which exhibits standing on two legs. Well before it is able to stand without support the human infant exhibits such adaptive-manipulative behavior as "combines two cubes." The chimpanzee, on the other hand, while "precocious" in gross postural behavior, fails to show this type of manipulative behavior until well into the second year of life. The animal tends to occupy himself with one cube at a time at an age which sees the human infant mature enough to hit cubes together or even to begin placing one on top of another.

Common to various species of primates, unquestionably because of underlying genetically determined common patterns of neuromuscular growth, are postural responses which appear during the first few months after birth. The tonic neck reflex, the whole series of changes in posture which lead to sitting, standing, and locomotion exhibit the appearance and disappearance of characteristic primate modes of adjustment to the force of gravity and to the supporting surface. Studies by Richter, Hines, Halverson and others have shown that the grasp reflex is strongest both in the rhesus monkey and in man at the ages of about 2 to 5 weeks after birth. Our observations on the chimpanzee also show that the maximum time of suspension of full body weight by one hand is within this age span. The "frog-like" position of the legs in the young infant lying down, the quadrupedal posture a little later, and the wide separation ("4 inches or more") between the feet in early bipedal standing suggest a common genetic background for man, ape, and monkey. Thus it is apparent that both similarities and differences between species reveal the dependence of function upon structural characteristics of the growing organism, the universality of which, either within species or between species, can only be explained by inborn neuromuscular organizations.

When it comes to finding an explanation for differences between individuals of the same species, the influence of environmental differences, and the interaction of environmental with innately determined factors in development become extremely difficult to disentangle. It is quite possible, however, to determine certain limits of variation which experimentally controlled modification of either set of variables may impose. Before going into our efforts to uncover these limits, I would like to refer to differences in postural development which appeared within the nursery-raised chimpanzee group.

Among 202 items dealing with postural behavior, 60 items of the Gesell and Thompson Behavior Examination were found to be applicable to the measurement of individual differences among the group of 12 chimpanzee infants. Although the group is small, an index of the reliability of this test of 60 items is indicated by the product-moment correlation of 0.95 obtained when scores of odd-numbered items were correlated against scores on even-numbered items.

Early postural development was found to be associated with early eruption of the deciduous dentition. The correlation here was 0.62, when progress was measured in terms of age from the date of fertilization. A positive correlation (0.60) also appeared between length of gestation and advancement in postural development. This evidence is more suggestive than final, because of the moderate level of statistical significance carried by this correlation, with our relatively small number of subjects. However, it leads to some interesting speculations as to the factors accounting for the relationship. Among the various possible advantages of a longer gestation time would be 1) the stability of the fetal environment, and 2) the better preparation for the ordeal of birth and for adjustment to the external environment in the longer term infant. On the other hand, a third set of factors might be the basis of the correlation found between the two variables we have measured. In this set would be included possible genetic differences which would affect both gestation time and rate of postural de-

velopment, or such early environmental factors as nutrition or toxicity.

The studies which I have discussed thus far have been in the nature of normative surveys, dealing with a population of animals for which conditions were kept as uniform as possible. The striking resistance of the rate and characteristics of postural development to rather marked differences in environment is exemplified in the fact that our nursery-raised chimpanzees showed no clear differences in this area from animals raised either by the chimpanzee mother, or from those given human love and affection by being raised in the homes of laboratory staff members. Apparently, drastic alterations from even these varied conditions would be necessary before the course of postural behavior development could be significantly altered. Common to all groups of subjects here under consideration were horizontal surfaces on which to crawl or creep, and supports from which the animal could pull himself to a bipedal stance. Given these supports, the self-initiated activity of the organism appears to insure the development of postural behavior according to a rather clearly defined schedule.

Beyond the area of postural behavior the different environmental opportunities could be seen to make more of an imprint. These data have not yet been fully analyzed and evaluated, but it seems clear that certain manipulatory skills are favored in the human home environment. As would also be suspected, rather specific social dependence relationships between chimpanzee and human being developed in these subjects,—relationships which were far from unilateral. This is a story which is still in process of enactment.

I would like to present next in considerable detail our studies of the effects of drastic alteration in the early visual environment.* There are theorists who regard adult visual perception as being only insignificantly affected by learning.[8, 6] There have also been those who went to the opposite extreme, emphasizing a relatively amorphous, non-reactive neonate, whose behavior is said to become organized entirely as the result of Pavlovian conditioning processes. Since the higher primate is a relatively helpless individual at birth, and requires a long time before complex discriminations and motor organizations appear, there has been plenty of room for speculating about the factors which are crucial in bringing about this increasingly intricate behaviors.

Ours is not the first attempt to eliminate experiential factors of one type or another, in order to determine what maturation alone can do. Tadpoles have been raised (notably by Carmichael) under anesthesia to prevent practice of swimming movements, and improvement in the absence of practice was demonstrated. Chicks and rats have been kept in darkness, with the result that growth of behavior controlled by vision was demonstrated in the absence of its use.[1, 7, 20] Children have been reared both under schedules of restricted training and with specially augmented practice, and again a basic maturational rate was demonstrated which limited the degree of retardation or advancement that could be produced by the training schedules.

Some studies carried out under this plan have revealed curious contradictions to the principle of movement in the absence of use. Cruze kept newly hatched chicks in darkness for 5 days and found them able to hit an average of 24 of the first 25 grains that were visually presented to them, which represented a reduction in errors over newly hatched chicks of 12 per cent. However, Padilla[15] found that if the period of darkness was extended to 14 days the pecking response failed to appear, presumably because the instinct to peck at spots on the ground died out through disuse, and the chicks began to starve in the midst of plenty. Thus, lack of practice of behavior which is basically instinctive or reflex in nature may result in maladaptations.

Human patients operated upon for con-

* The cooperation of Dr. W. J. Knauer M.D., of Jacksonville, Fla., who made the ophthalmoscopic examinations, and of H. W. Nissen, Ph.D., Josephine Semmes, Ph.D., and Kao-liang Chow, Ph.D., who joined in executing various phases of this study, is gratefully acknowledged.

genital cataract have provided significant clues as to the effects of disuse of vision in man.[19, 2, 22,23] The degree of lens opacity in these cases has ranged from that permitting color discrimination and some localization of light to the bare ability for telling day from night. In his review of these cases Senden has summarized the points of agreement to be found in the variety of records that are available. They show that there is an immediate awareness of a change following successful operation. They indicate that the patient is able to perceive the presence of a figure in the visual field, as distinguished from heterogeneous background, but the indication of the figure or a description of its shape is impossible. With a little practice the naming of colors usually appears first, within a matter of days. From this point on progress is slow, often highly discouraging, and some patients never get beyond the ability to identify terms of brightness and color. Others, over a period of months and even years, develop sufficient ability in form discrimination to identify simple geometric figures, read letters and numbers, and, in rare cases, to identify complex patterns such as words, outline drawings, and faces. Prior to the attainment of this last facility, the patients go through a long period of picking out isolated elements in the complex and inferring identities from these, often erroneously. For example, a child of 12, some months after operation, is reported by her doctor to have pointed to a picture and called it "a camel, because it has a hump". What she identified as a hump was the protruding dorsal fin of a fish.

In evaluating evidence from cases of congenital cataract it is necessary to take into account not only the degree of previous blindness, but also the degree of optical correction that is possible in the absence of the lens of the eye. And to this must be added the apparently universal handicap imposed by jerking movements of the eyes—the so-called spontaneous nystagmus. The effects of these combined difficulties are not readily calculable. For this reason it would be highly desirable to eliminate these factors experimentally, if possible. The use of human subjects for such an experiment would be difficult to justify, quite obviously, because of the risk of producing irreparable visual handicaps.

In 1942 one infant male chimpanzee was separated from its mother on the day of birth and blindfolded with a gauze bandage and adhesive tape. This animal defeated the purpose of the experimenters by developing a knack for loosening the tape at the side of its left nostril, and habitually peeking down his nose with the left eye. By the age of 16 weeks he gained full freedom from facial bandages. Although he did not recognize his feeding bottle at this time, nor show fixation of persons or objects, he developed fairly adequate visually mediated behavior within a few weeks. At about the age of 2½ years this animal began to show a marked convergent squint, which persists to this day.

In 1945 two newborn chimpanzee infants, a male and a female, were housed in a completely darkened room. An electric lamp was turned on for brief intervals (45 seconds) several times daily in the routine care and feeding of these two infants. The degree of visual incompetence of these two infants when first tested at the age of 16 months was extreme.[17] They both showed intermittent bursts of spontaneous nystagmus, and were unable to fixate any objects in the visual field.[16] They were kept on a limited light schedule until one was 21 and the other 33 months of age. Beginning at 16 months of age, observations were made on both of these subjects to determine the nature of reflex responses to light and to follow the course of changes in behavior at a time for daily testing. Reflex responses which were present from the beginning included constriction of the pupil to light, startle responses to sudden changes of illumination, and "following" movements of the eyes (optokinetic nystagmus) in response to the motion of a large striated field.[9, 10] The animals also turned their eyes in the direction of a light in a dark room. If a glowing flashlight bulb was moved from side to side before their eyes, jerking movements of the eyes occurred, and the head also rotated in the direction of the

moving light. These reflex manifestations indicated that the eyes were at least sensitive to light. It was therefore an entirely unexpected finding, when ophthalmoscopic examination of the eyes was made, that the retina and optic disc, especially the latter, did not reflect as much light as do normal chimpanzee eyes. This observation remains unexplained, but is of interest in connection with changes in light reflectance with shifts in visual attention reported to occur in human children (Arnold Gesell and associates of the Yale Clinic of Child Development).

Both of these chimpanzees, identified in our records as Snark and Alfalfa, failed to show any visual responses to complex patterns of light until after they had spent many hours in illuminated surroundings. They did not respond to play objects or their feeding bottles, although these were usually promptly oriented to and grasped if the objects touched some part of the body. They did not blink if a blow toward the face was threatened. If an object was brought slowly toward the face the first reaction was a startled jump when contact occurred.

Alfalfa gradually developed normal recognition of objects, blinking to threats, and the cessation of startle to touch, all requiring a period of many months after she was moved into daylight surroundings. Snark learned to discriminate, after many hundreds of trials, large signs differing in color or pattern, which indicated either food or mild electric shock. These discriminations were learned between the ages of 20 and 27 months, before he was permanently moved into daylight surroundings. A test of visual acuity showed that this animal was also subnormal in this respect. Lines and spaces had to be wider than 3 mm. for him to distinguish horizontal from vertical stripes at 45 inches distance, where normals readily discriminated lines of 1/3 mm.

So far as was previously known, light stimulation is not essential to the normal growth of the primate retina or optic nerve.[14, 5] Yet this seems to be one possible explanation for the present lack of visual function and the pallor of the optic discs in Snark. That such a requirement for light is the explanation for all of the findings with these two chimpanzee subjects, and for the visual difficulties of human congenital cataract patients, is ruled out by several lines of evidence. In addition to the fact that congenital cataract patients have excellent color discrimination (and, incidentally, do not show pallor of the optic disc), we now have clear evidence from chimpanzee subjects that opportunity to make responses to *patterned* visual stimulation is essential to normal visual development.[21] This evidence was obtained in the following way:

Three additional newborn chimpanzees were put into the darkroom. Debi was raised for 7 months in complete darkness. (All routine care was done in darkness, except that once a week this infant was brought out for weighing while blindfolded). Kora was raised for the same period on a schedule which provided an average of 1½ hours of light daily through a white "Plexiglas" mask admitting only diffuse, unpatterned light. The remaining hours of the day she was in darkness. Lad was given 1½ hours of patterned light daily. For example, he could observe the edges of his crib, the variations in pattern introduced by movements of his own body and appendages, and all the accompaniments of bottle feeding, including the moving about of persons in the moderately lighted room.

With some minor exceptions described below, the behavior of Debi and Kora, upon removal into daylight surroundings at 7 months of age, was similar to that which has been illustrated for Snark and Alfalfa. Debi, following total light deprivation, did show pallor of the optic disc, but to a lesser extent than Snark or Alfalfa. Kora did not show this. The rates of acquisition of responses to complex patterns of light and to movement in the visual field are indicated by the following tabulation (numbers refer to the number of days after removal into daylight surroundings before the behavior appeared):

Amount of light, per day, during first 7 months after birth	Debi none	Kora 1½ hours, unpatterned	Laa 1½ hours, patterned
Blink to object moving across field of vision	15	6	0
Visual pursuit* of moving person	30	13	0
Vis. pursuit* of moving bright colored toy ..	13	13	0
Vis. pursuit* of moving feeding bottle	16	20	0
Fixation of still person	30	13	0
Fixation of person's hand	24	20	0
Mouth approach toward bottle	27	20	0
Avoidance of strange object	33	38	2

*"Pursuit" was a series of re-fixations, not steady following as in normal animals of comparable age.

By 7 months of age Lad's visual performance was indistinguishable from that of normally raised chimpanzees.

The differences between Debi and Kora indicated by these figures may not lie outside the range of variation that would occur in a group of animals treated exactly the same as either Debi or Kora. This question could only be checked by repeating the experiment many times.

Between 7 and 10 months of age Debi and Kora both showed an intermittent outward (wall-eyed)) deviation of the eyes, moderate in degree, which gradually was overcome. Both infants also showed an initial spontaneous nystagmus, which appeared sporadically, and was more pronounced under general excitement than when the animals were well relaxed. Covering one eye caused the eyes to jerk rapidly toward the side of the open eye, return slowly, and repeat the cycle continuously. This curious maladaptation (from the point of view of good vision) continued for several months. Lad showed neither of these difficulties.

Whereas normal animals of 7 months learned to avoid a large yellow and black striped disc after receiving 1 or 2 mild electric shocks from it, Debi and Kora were shocked from it twice a day for 6 and 9 days, respectively, before they so much as whimpered when it was shown. It was 13 (Kora) or 15 (Debi) days before they consistently indicated by some sort of avoidance response that they saw the disc within 5 seconds of the time that it was raised in front of their eyes.

Since we saw earlier that certain types of instinctively given visual responses die out if they are not put to use, it is still conceivable that 7 months of age is too late to reveal responses which might mature earlier than this in the chimpanzee. Accordingly, another infant chimpanzee, Kandy, was put in the darkroom for only the first 3 months of life. Her progress through the same sequence of observations, following removal into daylight surroundings, was approximately parallel to that of Debi and Kora. There were three interesting differences: 1) Kandy showed convergent squint (cross-eyes) which cleared up in a little less than two months. 2) She did not have spontaneous nystagmus. 3) She required 24 days, as compared with 13 or 15, to develop consistent avoidance of the black and yellow shock-disc. That this last difference may be a function of age is strongly suggested by the fact that an infant of 2 days was started through the same training, and failed to show avoidance in a months' time.

In addition to demonstrating the need for putting vision to use if it is to develop normally, the observations reported above indicate that growth factors, independent of practice, do operate in the early postnatal period. The darkroom animals, for example, were blinking to the movement of objects across the visual field within about two weeks after they began to live in daylight surroundings. The normally reared nursery animals do not begin to show this response until after they have reached 2 months of age. A little later they also begin to blink when an object approaches the face, and finally they cease blinking when movement is across the visual field, and blink only in response to movement toward the eyes. This differentiation (of movement *across* from movement *toward*) required upwards of 2 months of

of post-darkroom experience in Kandy, Debi, and Kora.

As a final indication of the complexity of interrelated factors which cooperate in the development, and maintenance, of normal visual functions in higher primates, the experiment with Faik may be cited. This animal was raised to 7 months of age in the normal daylight routine of the Laboratories' nursery. He was then put through the series of observations indicated above, including a test of visual discrimination learning. He had excellent use of vision. At 8 months he was put into the darkroom. He lived an active life filled with tactile, auditory, olfactory, gustatory, and kinaesthetic stimulation. He invited "rough-house" play from his caretakers at feeding times. He was brought out once a week, blindfolded, for weighing and examination of hair and skin condition. He had always been, and continued to be, smaller than the average infant of his age, but his general state of health was entirely satisfactory.

At the age of 24 months this animal was returned to daylight living quarters. He had lost all ability to utilize vision in his interplay with the environment. He no longer recognized the feeding bottle, failed to look at objects or persons, either stationary or moving. More than this, he possessed a strong spontaneous nystagmus and was even unable to follow a moving light in a darkroom until the 5th day after he was reinstated into a lighted environment. This first following, as in the early "following" movements of all the inexperienced subjects, was not following in the sense of smooth pursuit movements, but a series of jerky refixations.

Even in direct sunlight Faik failed to grimace or show lid closure. Newborn infants, Kandy at 3 months and Lad and Kora at 7 months (Debi was unfortunately not tested) exhibited lid closure in such intense light, but Faik gave no indication of the slightest discomfort when the sun shone in his eyes. Faik showed pallor similar to that of Snark and Alfalfa in his optic discs. His recovery of vision has been slow and is at the present time only partial. The more complete explanation of his case, and that of Snark, remain a challenge to further research.

General Conclusions

1. Behavior patterns make their appearance at characteristic age levels, sometimes as a function of gross structural factors such as skeletal proportion.

2. Developing behavior patterns show variation within a range that is limited by genetic factors. The operation of these genetic factors and the limits imposed by them are only partially understood.

3. Among non-genetic factors in development, such as nutrition, temperature range, exposure to pathogens, and stimulation to sensory-motor exercise, the last (that is, the arousal of behavior) appears to be of increasing significance the higher one goes in the phylogenetic series.

4. Visual perception in higher primates involves a complex sensory-motor process which develops as a result of interaction between maturational and environmental variables. Deficiencies in either class of variable affects the operation of the other in a predictable manner, and beyond fairly narrow limits will produce behavior anomalies.

REFERENCES.

1. Cruze, W. W. Maturation and Learning in Chicks. J. comp. Psychol., **19**, 371-409, 1935.
2. Dennis, W. Congenital Cataract and Unlearned Behavior. J. genet. Psychol., **44**, 340-351, 1934.
3. Foley, J. P. An Experimental Investigation of the Effect of Prolonged Inversion of the Visual Field in the Rhesus Monkey (Macaca mulatta). J. genet. Psychol., **56**, 21-51, 1940.
4. Gesell, A., Ilg. F. L., and Bullis, G. E. Vision, its Development in Infant and Child. New York: Paul B. Hoeber, 1949
5. Goodman, L. Effect of Total Absence of Function on the Optic System of Rabbits. Amer. J. Physiol., **100**, 46-63, 1932.
6. Hebb, D. O. The Organization of Behavior: a Neurophysiological Theory. New York: John Wiley and Sons, 1949.
7. Lashley, K. S., and Russell, J. T. The Mechanism of Vision: XI. A Preliminary Test of Innate Organization. J. genet. Psychol., **45**, 136-144, 1934.
8. Leeper, R. A Study of a Neglected Portion of the Field of Learning—the Development of Sensory Organization. J. genet. Psychol., **46**, 41-75, 1935.
9. McGinnis, J. M. Eye Movements and Optic Nystagmus in Early Infancy. Genet. Psychol. Monogr., **8**, 321-430, 1930.
10. Mowrer, O. H. "Maturation" vs. "Learning" in the Development of Vestibular and Optokinetic Nystagmus. J. genet. Psychol., **48**, 383-404, 1936.
11. Nissen, H. W., and Riesen, A. H. The Deciduous Dentition of Chimpanzee. Growth, **9**, 263-274, 1945.
12. Nissen, H. W., and Riesen, A. H. Onset of Ossification in the Epiphyses and Short Bones of the Extremities in Chimpanzee. Growth, **13**, 45-70, 1949.

(Continued on page 32)

LEGAL MEDICINE OF BLOOD GROUPS

Individual Diagnosis of Bloodstains*

By LEONE LATTES, M.D.**

More than thirty years ago, when I wrote my first book and began the study of the blood groups recently discovered by Landsteiner, I discussed them from the point of view of the general concept of biochemical individuality. Now, many years later, the term "blood groups" has no longer but an historical interest, as the four classical blood groups constitute but one among several systems that make up the biochemical individuality. This individuality is not limited to the blood, but can be found in all the cells and fluids of the organism and it poses problems of enormous biological interest. To these problems the discovery of the Rhesus system has added the problem of "the conflict of individualities" (in pregnancy or transfusion).

I will discuss these subjects only very briefly, and it would indeed be superfluous to do more in a country where a whole theory, with a wealth of most varied applications, was developed and has flourished. I shall limit myself to those aspects of biochemical identity that are relevant to medical jurisprudence; and I am all the more pleased to do so, as I take pride in having contributed in this field something new and useful.

The oldest of all problems dealing with biochemical individuality is that of the identification of blood stains, formerly called the individual diagnosis of blood stains and its relation to the so-called generic and specific diagnoses. The problem is far from new, as it seems to have been mentioned already in Chinese antiquity. In the nineteenth century attempts were made to identify the individual by the smell of the blood after treatment with sulphuric acid, a method conceivably within reach of the sense of smell of a dog, but certainly not of man.

The scientific phase of individual diagnosis started with the discovery of blood grouping by Landsteiner, which dealt a mortal blow to the dogma of homogeneity of the blood and humors within the human species. This dogma was so deeply rooted, that many continued to consider the reactions between man and man, that is, the isoreactions, as pathological. Landsteiner had the genius to explain them on the basis of the differential physiology of human groups, and to point out the possible applications of his discovery to the clinical problems of transfusion and to the legal medicine of bloodstains. His first publication on this subject appeared in 1903 in collaboration with the German court physician, Richter. It is however not exact to say, as many have said, that the group of blood stains had been determined for the first time, as this work was purely experimental and proved only that the agglutinins may be preserved in dried blood. This discovery suggested that extracts from a bloodstain be tested with red cells of a criminal suspect, so that in case of agglutination, the identity of the blood in the stain with that of the suspect could be excluded. This Landsteiner-Richter test was published in a small and now almost unobtainable German journal, and did not stimulate any interest in medico-legal circles nor did the almost simultaneous publication of Boff who expressed the same idea. In 1913 I began to study the issue once more and in 1916 for the first time introduced a practical, medico-legal individual diagnosis of bloodstains in court. The medico-legal methods which I have developed have never been modified significantly. Since then, I have recommended the investigation of the agglutinins and of the agglutinogens by means of selective absorption of the agglutinins. I emphasized that this method allows a double check, and that while the investigation of the agglutinins can be successful even with very small bloodstains, that of the agglutinogens is of more general use, because the agglutinogens are much more resistent to destructive processes than the agglutinins, and because they are

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present in secretions and organic matter which contain no agglutinins, such as sperm and saliva. In this field also, a fortunate coincidence allowed me to be the first to act as a judicial expert. It concerned a case of homicide in which I succeeded in identifying the smoker of certain cigarettes by means of the residue of saliva.

In the same way, I succeeded, several years afterwards, in identifying the author of anonymous letters through an examination of the glued edges. The methods used then are still in use, although with some basic improvements such as the introduction of quantitative measurements, and certain controls made necessary by the discovery that the materials stained with blood may absorb or destroy the agglutinins either intrinsically or because they are impregnated with cutaneous secretions. Finally, it should be mentioned that the demonstration of the agglutinogens has, of course, been extended to other antigens especially the M and N and more recently the Rh.

The individual diagnosis of stains not only of blood, but of any secretions for judicial purposes is now routine in many official institutions. For example, the F.B.I. Laboratory, during the last few years has investigated thousands of objects related to crimes and originating from all over the United States. This type of centralized organization which exists also in Egypt, in Chile, in Denmark, and I believe, also in Germany, Russia, Belgium, Poland and England, permits the study of many thousands of cases and, therefore, allows one to get a general view of the problem, to improve technical procedures wherever possible, and to subject the judicial interpretation of results to scientific criticism.

The established points of departure remain essentially the following:

1. The group substances (antibodies and antigens) may be found in dried blood and in most secretions.

2. Generally, auto-agglutination does not occur, which means that if under proper conditions the extract of a blood stain agglutinates the cells of a given person, the blood stain cannot be from that person.

3. The specific group antigens are fixed constitutional properties and show no qualitative variation during the lifetime of an individual.

The possibility of reaching a medico-legal identity diagnosis is due to the fact that damaging influences do not necessarily affect the reacting substances to such a degree as to make the reactions impossible. Thus, for example, the beginning purefaction does not alter the agglutinins or the agglutinogens significantly, so that the determination of the group can be made after death from the pericardial fluid, fluids from blisters, the content of the seminal vesicles, etc. Moderate heating does not affect the iso-agglutinins and the agglutinogens keep their specific absorbing qualities even after heating to the boiling point. Thus the circumstances often leave side possibilities to the investigator, but these are such that, except in special cases, negative results cannot be considered proof, for even if the stain should appear relatively intact grossly, it still may have suffered such intrinsic changes as to make it unsuited for iso-reactions.

There are two ways of arriving at an individual diagnosis from a stain. The first consists of demonstrating the iso-agglutinating properties of the dry serum; the second, of demonstrating the absorptive properties of the cellular material, that is, the presence of specific iso-agglutinating substances. In view of the importance and delicate nature of the cases in medico-legal practice, whenever possible, both methods should be used.

Under certain circumstances all sera can produce a pseudo-agglutination of red blood cells which is not much different from that obtained with mineral colloids, and is due to the formation of rouleaux. This cause of error hinders the investigation considerably, especially in the examination of traces of material. This difficulty can be overcome by the use of special techniques. Often, however, the diagnosis of stains must be based only on the examination of agglutinogens, as the agglutinins do not exist at all

(group AB, new born, etc.) or have been destroyed by drying, cooking, etc. In this case, the possibility of pseudo-agglutination does not matter. The agglutinogens cannot be demonstrated directly, but only through indirect methods. This can be done by means of the selective absorption of the agglutinins in a diagnostic serum by the cells of the blood under examination. The agglutinins anti-A or anti-B are absorbed and fixed by the cells, and their disappearance from the serum can be measured by titration. This gives an adequate quantitative measure of the specificity of the absorption, even when it is only partial.

In practical criminological cases the problem is not a biological, juridical or procedural one (except, perhaps, that of the right to obtain the blood needed for the tests) but rather a technical one, namely in what way and with what degree of certainty the group-specific properties of a stain can be determined. This is a long and delicate task calling for specialized investigators who must have the necessary controls organized in advance. It is not surprising, therefore, that some magistrates still hesitate in admitting this kind of evidence.

Let us examine to what extent they are justified. One must, first of all, differentiate failure from errors for they are of very different logical nature and practical value. The possibility of failure is unavoidable; lack of sufficient organic material, its age, its bad state of preservation and even its alteration by the surroundings may make the task impossible. However, this is not in itself enough to destroy the intrinsic value of the method. Technical failure, if properly evaluated, does not cause judicial error; it only deprives the judge of an element of proof, which is of course far less dangerous. One must not confuse lack of results with negative results. For example, failure to find isoagglutinins in a blood stain is not valid proof that one is not dealing with blood of the AB group. Only positive reactions have any value as proof. Negative results are often logical complements of positive ones, but only in exceptional cases are they in themselves an element of probability. As a rule, they amount to failure, that is, the impossibility of drawing any conclusion, a fact which is not of great judicial importance.

The crucial question is not that of the possibility of failure, but of error, namely, of arriving at positive but erroneous conclusions which may lead to judicial errors. This may be due to intrinsic defects of the method or to the fact that the investigator did not apply it correctly. In addition to these difficulties, magistrates have been discouraged by unfortunate statements made by such eminent specialists as Ludvig Hirszfeld to the effect that the group problems have not been sufficiently studied, as yet, to serve the ends of practical criminology and that one must be optimistic in regard to the future application of group investigation to criminology. It seems to me, however, that the distinguished biologist Hirszfeld does not consider the medico-legal problems in their full scope. When he expresses the opinion that the group investigations are not usually worth the necessary effort, he overlooks the fact that, in matters of guilt or innocence, no effort can be considered excessive. The magistrate cannot neglect the chance that the proof obtained might constitute certainty, even if remote. The dramatic case cited by Hirszfeld to demonstate the inadequacy of the test, demonstates, on the contrary, the inadequacy of the expert. The stains in the clothes of the accused were found to contain the agglutinin anti-B and not the anti-A. The accused belonged to group O, which contains normally both anti-A and anti-B. The victim belonged to group A. The expert attributed the stains to the group A of the victim and the accused was condemned to death. The experts had committed a logical rather than a technical error. For the agglutinin anti-B found in the stain existed both in the blood of the accused and of the victim, and not having found the agglutinin anti-A in the stain was not sufficient grounds for a conclusion of such consequence. The absence of agglutinin anti-A may have been due to its disappearance from the stain

due to aging or to selective atrophy. The latter was indeed the case, as Hirszfeld himself was able to prove later. The results of the examination of the stain, although technically correct, could not constitute a proof, but at most, circumstantial evidence. Had the accused belonged to group B instead of O, the presence of agglutinin anti-B in the stain would have been absolute proof that the blood in the stain was not his.

Hirszfeld's great contribution was the discovery that, due to skin secretions, group substances may be found on clothes in places other than in the blood stained areas. It has also been shown that porous materials of all kinds, such as cloth, paper, etc. may cause non-specific absorption. These investigations have taught how to avoid important technical errors, not logical ones in this case. Another source of error is the fact that some of the more common animals (pigs, horses, rabbits, etc.) have certain group specificities similar to the human ones. Suspected contamination with animal blood or secretions must therefore be ruled out with specific sera.

Despite these difficulties, it seems to me that Hirszfeld and others, such as Sandoval, are unduly pessimistic. When Hirszfeld, in support of this statement that group criminology is still inadequate, refers to the finding of his pupil Popielsky that washing with cold water eradicates the group properties of fresh stains, he obviously exaggerates, for how is one to find the group in blood that no longer exists? It would be as much as to attempt to demonstrate a heart ailment in the ashes of a cremated corpse and then complain that autopsy is an inadequate method! The fact is that stained objects are sometimes easy, sometimes difficult to examine. Some, as freshly clotted blood are very easy and the police, who are first on the scene of crime, should always have suitable receptacles for preserving fresh blood traces. It is also relatively easy to examine large amounts of blood dried rapidly on an impermeable surface without denaturing chemical action. In these cases, one may achieve the two complementary diagnoses of agglutinins and agglutinogens. In my personal practice, this situation has often presented itself when examining stone, glass, straw, weapons, etc. These are the cases in which specific or non-specific absorbent properties of the material do not have to be taken into account.

Objects made of absorbent material, however, present greater difficulties. Stains on cloth, for instance, may often allow only the determination of the agglutinogens. At times, the picture is rather complex (admixture of blood and body fluids of more than one individual, or of animal and human blood, absorbent power of the material itself, etc). The situation is even more difficult with absorbent bases that exert a chemical action on the group properties (leather, lime, rust, soft wood, soap, etc.). Lastly, one often meets with complete failure (blood that is scanty or old). In other words, independently of the technic, the test may be a failure or a complete success, according to the circumstances and the nature of the object. From the judicial point of view this means that the investigation may have no value at all as proof, or may furnish circumstantial evidence with greater or lesser degree of probability or, finally, it may furnish incontrovertible proof. This is not surprising, for it is not different from other means of seeking proof.

The judiciary, far from accepting only decisive means of proof, takes advantage also of indications and probabilities, and it would be a mistake to reject them *a priori*. In individual cases it is the expert's duty to choose the appropriate technique, endeavor to avoid mistakes and increase the degree of probability and, if possible, reach certainty. There are cases in which exceptional intrinsic difficulties make obvious from the outset that certainty cannot be reached, but there are other, easier cases in which one is heartened by the knowledge that, through appropriate techniques correctly applied, it is possible to obtain complete success.

What constitutes certainty? Here again it is a matter of degree. Absolute certainty consists of the complete determina-

tion of the group; that is to say, the independent and complementary demonstration of the agglutinins and the agglutinogens. If in a human stain one demonstrates the presence of A and anti-B, and the absence of B and anti-A, one may be quite sure that the blood in question belongs to group A. Under favorable circumstances, one may also arrive at the demonstration of the subgroups A_1 and A_2 (Boyd and Bouyd, Therkelsen, Harley). These are the cases in which the negative results harmonize with the positive ones.

There is another, more limited, kind of certainty: that which is obtained when cross-testing cannot be carried out. It may happen that there is only a very small, fresh, compact crust available, such as a stain on the point of a needle, in which the amount of blood does not suffice for the determination of the agglutinogens, but is barely enough for a spectroscopic examination, a specific test of capillary precipitation, and the search for agglutinins by my microscopic method. Similarly, we may have to deal with impregnated, old or fixed blood, which does not allow the determination of the agglutinins, but only that of the agglutinogens. Success, in these cases, consists of the positive determination of one or the other of the group elements, anti-A, anti-B, A or B. This is also a certain result, although without the same degree of the certainty of the blood group determination. The certainty is limited to the existence of the group element. If, for example, one finds anti-A and not anti-B one cannot establish with absolute certainty that the blood is of group B, since anti-A is present in both group B and group O; one can only say that the blood is not A or AB, as the absence of anti-B may be intrinsic or due to the fact that this agglutinin has disappeared for one reason or another. The degree of probability here depends upon the circumstances and may amount even to absolute certainty if the blood is very fresh. In arriving at an opinion, we must bear in mind that the agglutinins may disappear, together or separately, much more easily than the agglutinogens. In any case, the relative certainty of a group element can never become the absolute certainty of the group, as this would clearly be a logical error.

The same reasoning holds for the determination of the group specific substances M and N in blood stains, which has been carried out with success by Matta, Wiener, Clausen, Muller and Christiaena. In this case one cannot expect to find non-existent antibodies. Moreover, while it is easy to determine the property M by the absorption of the specific antiserum, the determination of N, where the absorption is less specific, may leave some doubts. The determination of the substances Rh in the stains has likewise been attempted with the same procedure (Wolff, Closon), but the investigation is only in its early stages.

The mere fact that A and B are not found does not mean, as a rule (except when M or N are found), that we are dealing with group O, but only indicates greater or lesser degree of probability, according to circumstances. The preparation of anti-O serums of constant action, with which one could demonstrate positively the presence of the property O, would obviously be a big step forward, but this has not yet been achieved.

Finally, in other cases, one does not deal with failure of the test, but with doubtful results. This is a technical possibility. The fundamental test is the determination of agglutinogens, which is done by quantitative absorption of isoagglutinins. The presence of agglutinogens is shown by the fall in the agglutinating titer of the specific serum. Now, one must not forget that quantitative determinations are never absolute, even when carried out under the best conditions; they all contain a margin of error. In the titration of agglutinating serums the margin of error is significant. The procedure generally consists of progressive dilutions in four successive tubes. Under suitable conditions, one may obtain agglutination in all four tubes, that is to say, obtain a qualitative inhibition. However, it may happen that, if the amount of material is small or badly preserved, its power of absorption is weak and agglutination oc-

curs only in the first tube. This means that the fall of titer occurs only in three steps. Diagnosis is still possible but with less certainty. The degree of certainty is even less if the fall is only two steps, whereas, a fall of only one step (positive agglutination in the three first tubes) is within the margin of error of the method. Thus, the answer may be: proof, probability or circumstantial evidence.

The important thing is not to force the meaning of the results, but present them faithfully to the judge, whose task it is to evaluate them for the purposes of a legal decision. One should not expect more of this investigation than it can offer. It would also be unjust to overlook the value of indications or probabilities, as the case may be, just because they do not amount to conclusive proofs.

The group diagnosis of stains of blood or secretions is not in itself the object of the investigation, but is made for purposes of comparison. If the victim and the accused belong to the same group, an examination of the stains, even if successful, would, of course, be useless. It has been calculated (Wiener) that, for the white race, the chance of victim and accused belonging to different groups (favorable combination for a judgment), is as high as 65% if one considers only the ABO system. In other words, one may expect varied degrees of success in 2/3 of the cases. In addition, the factors M, N, P, Rh, and others less well known, may considerably increase the probability of success.

In many instances the problem is easier to solve as one does not have to choose between two persons, say, victim and accused, but to seek identification, as in the case of a burglary in which the burglar has been wounded. Need we point out the value of knowing that the author of a crime has fair hair, despite the fact that there are many fair-haired people in the world? Likewise, if the dumb but eloquent testimony of a bloodstain tells us that the burglar belonged to group B, or that he has an A eliminator in his saliva, this information may be very important in the identification of the guilty person, either by coincidence or by exclusion. The possibility of coincidence is not the fault of the method and must be interpreted in the light of other evidence if one is not to expect of the method more than it can offer. Judicial results reported by various writers show how valuable are the services the method can render.

The judicial and social importance of criminal investigation is so great, that one should use every possible method to establish the truth. The fact that success or failure of the method cannot be predicted in individual cases should not be an obstacle to its systematic application.

BIBLIOGRAPHY

LATTES:
Various papers on blood groups in stains published in the "Archivio di antropologia criminale e medicina legale", 1913, 1915, 1916, 1925, 1930, 1932, 1933.

id. Praktische Erfahrungen ueber Blutgruppenbestimmung in Flecken. Vierteljahrs. gerichtl. Mediz. 1927.

id. Les groupes sanguins en medecine legale; Congr. francais de med. leg. in "Annales de med. leg., 1927, 1933."

id. Blutgruppendiagnose von Blutflecken. Ukrain. Zentralblatt f. Blutgruppenforschung., 1928.

id. El diagnostico individual de las huellas sangrientas y no sangrientas. Archivos de med. leg. Buenos Aires, 1939.

id. Sobre la investigacion del grupo sanguinea en las manchas. 2o congreso fur die forensische Praxis. Zeitschr. f Medizinalbeamte. 1903, XXVI. 85.

Amado Ferreira. Diagnose individual das manchas de sangue. Bol. Inst. Oscar Freire, Sao Paulo. 5. junho 1949.

Holzer. Ein einfaches Verfahren zur Gruppenbestimmung an vertrocknetem Blut durch Agglutininbindung. Deutsch. Zeits. gerichtl. Med. 1931, XVI 445.

Hirszfeld. Les groupes sanguins. Masson & C. Paris, 1938.

Therkelsen. Typenbestimmung bei gerichtlich medizinischen Fleckenuntersuchungen. Zeitschr. f. Rassenphysiologie. 8. 98. 1936.

White Briggs. Controls in grouping bloodstains. First american medico-legal Congress. St. Jouis, jan. 20, 1948. F.B.I. Bull. sept. 1949 (see also dec. 1947).

Wiener. Medico legal applications of blood grouping. Vida neuva (Habana), vol. 40, 197, 1940.

Wolff. Les groupes sanguins et les facteurs MMP et Rh au point de vue medico-legal.

Closon. L'antigene Rh dans le sang desseche. Congres internat. de medecine legale. Liege, 1947.

DIAGNOSIS AND MANAGEMENT OF PROGRESSIVE CONFUSION BEYOND MIDDLE AGE

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The years that have elapsed since the cutting of the umbilical cord can hardly be an exact index of an individual's biologic age; they furnish only a rough estimate of the alterations that have occurred in the tissues of the organism. It cannot be presumed beyond statistical probabilities that a given individual at a given age suffers from the afflictions common to that age. Furthermore, tissue degeneration may be a selective process that progresses unevenly so that a rapidly deteriorating brain may be coupled with a well preserved myocardium.

With aging there develops a variable degree of arteriosclerosis, but severe arteriosclerosis is not an invariable concomitant of aging. Many patients reach the age of ninety with minimal vascular disease of the brain. Nevertheless, it is too often taken for granted that impairments of intellectual function which appear in older people are attributable to arteriosclerosis. Similarly it is often assumed that any mental confusion that appears past the age of fifty is a result of a deficient blood supply. This attitude glibly joins the diagnosis to the age, and naively assumes the decline of function stems only from an impoverished circulation; it results in a disregard of conditions for which there is a specific treatment, prognosis and management.

The psychic manifestations of organic brain diseases are similar regardless of the etiology. They consist of memory defects, loss of ability to think in abstract terms, constriction of fields of thought and interest, inability to analyze the elements of a complex problem or group diverse objects into appropriate categories; there are alterations in mood, preservation of ideas and activities, and impaired judgments. Confabulation, disorganized delusions and paranoid ideas serve to fill the defects and inadequacies produced by the brain damage. When a patient begins to demonstrate these symptoms, it is the responsibility of the managing physician to outline a course of investigation and treatment.

Among the most common causes of mental confusion are the vascular diseases of the brain such as develop with hypertension, diabetes and arteriosclerosis, and less frequently with periarteritis nodosa, polycythemia, and disseminated lupus erythematosus. The pathology consists of focal areas of encephalomalacia in the distribution of the vessels. The symptomatology is characterized by the sudden, apoplectic onset of neurologic defects that are most disabling at the time of the onset of the lesion and then gradually improve. Coupled with an organic type of psychological disturbance are other disabilities seen in the form of hemiplegias, hemihypalgesias, aphasias and visual field defects. Occasionally the only focal sign may be a brief period of mental confusion. The prognosis depends on the underlying vascular disease, but generally there is a considerable improvement following the first attack and many years may elapse before there is another similar ictus. Hence a period of physical and mental rehabilitation should be outlined to prevent disabling weakness, contractures and the deteriorating effects of inactivity. If repeated vascular lesions occur, the residual functional defect is more severe each time.

The other common cause of confusion in the elderly is the group of parenchymatous degenerative diseases of the cerebral cortex that constitute the senile and presenile dementias of the type associated with Alzheimer's and Pick's diseases. In these conditions there is a widespread loss of cortical neurons. There are characteristic histologic changes of the neurons apparently resulting from intracellular physico-chemical derangements. Secondary to this process is a proliferation of glia. These are insidiously developing, and slowly, unrelentingly progressive diseases with few objective focal neurologic signs be-

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yond those of organic dementia. These conditions create management problems for the families of the afflicted patients and ultimately the patient's mental deterioration requires a regime of custodial care. Among the rarer degenerative conditions that may also result in intellectual deterioration are Huntington's chorea, amyotrophic lateral sclerosis, advanced multiple sclerosis and diffuse sclerosis.

The most important infection to be considered in this age group is general paresis. The clinical manifestations may be only those of an organic dementia, but focal signs such as "strokes," tremors, ocular palsies, and seizures may occur. Early diagnosis and treatment with penicillin will result in rapid recovery in over eighty per cent of the cases. Other less common infections such as brain abscess, chronic and acute meningitis, granulomas of the brain, and the encephalitides should be investigated. Occasionally a spontaneous subarachnoid hemorrhage may cause fever, cervical rigidity and mental confusion and thereby be confused with meningitis.

Of the space occupying lesions one should especially search for a subdural hematoma and neoplasms. The subdural hematoma is characterized by a mild head injury which is followed some time later by the slow development of headache, confusion, choked disc and focal neurologic signs. Adequately treated, the subdural hematoma has an excellent prognosis. The search for a brain tumor should not be delayed until there are the advanced findings of choked disc and projectile vomiting, but should be initiated whenever there is evidence of a progressive focal neurologic lesion or unexplained seizures appearing for the first time in adult life. A large group of intracranial neoplasms are benign and even some malignant gliomas permit a long post-operative useful life for the patient. Therefore, all brain tumors should be investigated surgically because only in that way can many patients be rescued.

Many metabolic disturbances also result in mental confusion. Although typical pellagra is seldom seen now, pellagrinous mental states are seen associated with polyneuritis and other vitamin deficiency phenomena. They appear in penurious bachelors who rely on their own amateurish culinary resources and subsist on a diet of beans, bread and coffee. Pernicious anemia and severe secondary anemias may produce cerebral changes similar to pellagra. Hypothyroidism, marked hyperthyroidism, and recurrent severe hypoglycemia may result in severe brain damage. Cholemic and uremic states result in temporary and at times permanent brain damage.

The most important toxin leading to cerebral degeneration is alcohol, but drugs such as barbiturates and narcotics, lead, arsenic, aniline dyes and organic solvents are among the toxins also to be investigated.

Of course, organic cerebral states must be differentiated from functional disturbances such as schizophrenia, hysteria, and depressions. These seldom appear for the first time past middle age, but exacerbations of neurotic or psychotic behavior after a period of relative adjustment may be confused with organic brain disease. The differentiation between organic and functional states is entirely dependent on a careful psychiatric and social history and psychological studies such as a qualified psychiatrist can perform. The management of these functional states relies on measures to aid the patient in his emotional conflicts and personal and social maladjustments.

A routine of investigation to determine the cause of an organic mental derangement should include a careful medical and psychiatric history, a general physical and neurological examination, x-rays of the skull and chest, urinalysis, complete blood count and serologic reactions of the blood, electroencephalogram and spinal tap. Special attention should be given to the pressure, cell count, total protein, and serology of the spinal fluid. Beyond this there may be a need for pneumoencephalography, ventriculography, and angiography.

If there remains a permanent but nonprogressive neurologic defect, after the etiologic factors are treated, there should be developed a regime of mental, physical and social rehabilitation. This is to

be motivated not only by the desire to avoid having the patient become a burden on the family and society, but to prevent the demoralization into which chronic illness can inexorably drag even the strongest characters. A vigorous, enthusiastic program utilizing the combined services of the neurologist, physiatrist, occupational therapist and social worker can restore up to three-fourths of brain-damaged people to some social adjustment.

The management of the confusion *per se* depends on satisfying the patient's basic emotional needs while avoiding complex anxiety arousing situations. It has been found that frequent small feedings, or the oral gratification of smoking have a pacifying effect on some confused patients. Mild sedation may be necessary if there is excessive excitement, but if the patient is somnolent some stimulants, as amphetamine, may be used. A simple, regularly organized routine which is predictable from day to day avoids the disturbance engendered by the difficulty of coping with unusual and frustrating complexities of life. A close attachment to a single nursing attendant seems to aid in effecting a peaceful adjustment to the patient's limitations.

Summary

Although many older patients develop confusion as a result of vascular lesions of the brain, a spirit of resignation and hopelessness deprives these patients of the benefits of spirited program rehabilitation; and the presumption that confusion in the aged results from arteriosclerosis may lead to a failure to investigate other remediable conditions. A careful search should be made by clinical and laboratory methods to determine the cause of the confusion. After the etiology has been determined, a program of rehabilitation should be outlined if possible, and a simplified mode of existence developed for the irremediable cases.

BEHAVIOR

(Continued from page 23)

13. Nissen, H. W., and Yerkes, R. M. Reproduction in the Chimpanzee: Report on Forty-nine Births. Anat. Rec., **86**, 567-578, 1943.
14. Ogneff, J. Ueber die Aenderungen in den Organen der Goldfische nach dreijahrigem Verbleiben in Finsternis. Anat. Anz., **40**, 81-87, 1911.
15. Padilla, S. G. Further Studies on the Delayed Pecking of Chicks. J.comp. Psychol., **20**, 413-443, 1935.
16. Perlman, H. B., and Case, T. J. Mechanisms of Ocular Movement in Man: Influence of the Vestibular Apparatus. Arch. of Otolaryng., **40**, 457-467, 1944.
17. Riesen, A. H. The Development of Visual Perception in Man and Chimpanzee. Science, **106**, 107-108, 1947.
18. Riesen, A. H., and Kinder, E. F. Postural Development of Infant Chimpanzees. (in prep.)
19. Senden M. v. Raum- und Gestaltauffassung bei operierten Blindgeborenen vor und nach der Operation. Leipzig: Barth, 1932.
20. Turner, W. D. The Development of Perception: I. Visual Direction: the First Eidoscopic Orientations of the Albino Rat. J. genet. Psychol., **47**, 121-140, 1935.
21. Wald, G., and Burian, H. M. The Dissociation of Form Vision and Light Perception in Strabismic Amblyopia. Amer. J. Ophthalmol., **27**, 950-963, 1944.
22. Weill, G., and Pfersdorff, C. Les Functions Visuelles de L'aveugle ne Opere. Annal. Med. Psychol., **93** Pt. II. 367-382, 1935.
23. Weill, G., and Pfersdorff, C. Evolution Ulterieure des Facultes Visuelles d'une Aveugle-nee Operee. Strasbourg Med., **97**, 272-275, 1937.
24. Yerkes, R. M. Chimpanzees: a Laboratory Colony. New Haven: Yale University Press, 1943.

DIABETES

(Continued from page 6)

64. Kazal, L. A., Wolfe, E. K., Spicer, D. S., and Barnes, R. H., Proc. Soc. Exp. Biol. and Med., **74**, 8, 1950.
65. Candela, J. L. R., and Konig, W. C., Trabajos del Instituto Nacional de Ciencias Medicas, **18**, 31. 1950.
66. Waele, H. De., Arch. Internat. de Physiol., **55**, 209, 1948.
67. Waele, H. De., Arch. Internat. de Physiol., **57**, 133, 1949.
68. Pincus G. J., Proc. Amer. Diabetes Ass., **9**, 39, 1949.
69. Pincus, G. J., Proc. Soc. Exp. Biol. and Med., **74**, 377, 1950.
70. Sutherland, E. W., and Cori, C. F., J. Biol. Chem., **172**, 737, 1948.
71. Weisberg. H. F., Caren, R., Huddlestun, B., and Levine, R., Am. J. Physiol., **159**, 98, 1949.
72. Foa, P. P., Weinstein, H. R., and Smith, J. A., Am. J. Physiol., **157**, 197, 1949.
73. Morita. Y., and Orten, J. M., Feder. Proc., **8**, 230, 1949.
74. Foa, P. P., and Weinstein, H. R., Amer. J. Physiol., **163**, 711, 1950.
75. Foa, P. P., and Weinstein, H. R., Feder. Proc., **10**, 43, 1951.
76. Heard, R. D. H., Lazinski, E., Stewart, L., and Stewart, B. D., J. Biol. Chem., **172**, 857, 1948.
77. Dragstedt, L. R., Allen J. G., Julian, O. C., and Stinger, D., Amer. J. Physiol., **135**, 133, 1941.
78. Milla, E., and Trombetta, P., Boll. Soc. It. Biol. Sper., **23**, 97, 1947.

CLINICO-PATHOLOGIC CONFERENCE

Presented at Mount Sinai Hospital
Chicago, Illinois

Dr. H. J. Isaacs, Chairman
Dr. I. Davidsohn, Secretary

This 43 year old white male attorney was first admitted to Mount Sinai Hospital on July 21, 1947, with the complaint of right sided paralysis. He first noted impaired speech one week previously. This was followed in several hours by weakness of the right arm and leg. The symptoms became progressively more severe with complete right sided paralysis the next day. The patient reported slight dysphagia. No dizziness or headaches were noted at any time. A history of hypertension of indefinite duration was elicited. *Physical Examination* revealed blood pressure to be 210/110, pulse 80. A systolic murmur was heard at the apex and at the base of the heart. The liver edge was palpable 3 cm. below the right costal margin. Neurological examination revealed deviation of the tongue to the right, loss of nasolabial fold on the right, absent right sided abdominal reflexes, and increased deep reflexes on the right side.

Hospital Course: The patient followed an afebrile course and made a steady uneventful recovery. He was discharged after 41 days of hospitalization. An azotemia was noted during this stay.

Second Admission: The patient was readmitted to this hospital on October 19, 1949. He complained of weight loss, weakness, abdominal cramps, nausea, vomiting, headache, and pain in the left costovertebral angle with radiation to the left groin. For the past four months a mass had been noted in the left upper quadrant. The mass increased in size producing a sensation of pressure with abdominal enlargement on the left. Prior to this admission, on October 14, 1949, bloody urine was observed and persisted to the date of this admission. *Physical Examination* revealed a poorly-nourished pallid white male, who appeared chronically ill. Blood pressure was 150/90, pulse 100. The skin was dry, pale, and appeared icteric with a loss of tissue turgor. Dullness to percussion and decreased tactile fremitus were observed over the left lung base posteriorly. The heart borders were 10x20 cm with aortic configuration. A grade II to III systolic murmur was audible over the entire precordium. A mass filled the entire left abdomen and distended the left flank. The mass was nodular with a firm but cystic character. A similar but smaller mass, not distending the abdomen, was palpable in the R.U.Q. The masses were moderately tender; they did not move with respiration. On the 10th hospital day the abdomen was softer, nodularity of the mass was more pronounced, gross hematuria still persisted, and azotemia was progressive. On the 15th hospital day the patient developed precordial pain, parethesias in the upper extremities and a gallop rhythym. The patient still complained, on the 27th hospital day, of precordial distress with radiation down the left arm. On the 40th hospital day perforation of the nasal septum was noted for the first time. The urine became clear at this time. Nodules in the left sided mass would disappear and concomitantly gross hematuria developed. The blood pressure during the hospital stay varied between 125 to 150 systolic with an approximate diastolic level of 100. The patient was afebrile throughout his second admission. His course was progressively downhill. On the 57th hospital day oliguria developed. On the 58th day anuria was present. On this day the patient expired.

Dr. E. B. Freilich: In 1938, twelve years before this patient expired, I took care of his mother for polycystic kidneys. She died of uremia at the age of about 49. Realizing the familial tendency I urged that both her sons, one a lawyer, one a dentist, have I.V. pyelograms. Nothing

LAB. DATA:

BL. COUNTS:

	RBC	WBC	HB	STABS	SEGS	EOS	BAS	LYMPHS	MONOS	ABN.C	C.I
7-21-47	5.17	6,300	86.4%		79	2		12	4		.84
10-19-49	2.44	9,500	5.8 gms	0	76	0	0	22	2	0	0.79
11-15-49	2.28	5,000	7.0 gms	0	76	1	0	22	1	0	0.97
12- 5-49	3.8	6,800	11.9	4	76	0	0	20	0	0	1.02

BL. CHEM.

	SUGAR	NPN	UREA N.	T.P.	CHL.	ALB.	GLOB.	A/G	CHOL.	CO_2	CREAT.
7-21-47	106	62	38.9								3.4
8-20-47		77	33.4								4.3
10-21-49	118		179		544				188		
10-22-49		234.5	154.5								16.2
10-24-49				6.5		4.3	2.2	1.9/1			
10-28-49		300.	198								16.4
11- 4-49					554					35	
11-15-49			183								
11-21-49		268.5	170.5								11.7
11-28-49		307.0	162.5		552						12.3
12- 5-49		254	209		530						10.3
12-12-49		396	280.5								16.0

Oct. 21—Alkaline phosphatase—10.0 Ict. Ind. 3.5.

URINALYSIS:

	S.G.	REACT.	ALB.	SUGAR	WBS	RBC	
7-28-47	1.010	Acid	Tr.	0	2-4/HPF		
8- 4-47	1.005	Acid	Tr.	0	Rare		
8-25-47	1.012	Acid	Tr.	0	Occ.		
10-20-49	QNS	6.0	3+	0	0	Full Field	
11-17-49	1.013	5.5	Tr.	0	20-25	50-75	1 Bacteria
12- 1-49	1.012	Acid	Tr.	0	18-20	0	amorph. cryst.
12- 8-49	QNS	5.5	Tr.	0	5-8	10-20	

SEROLOGY:

7-22-47 Kahn—Neg.
10-19-49 Kahn—Neg. Kline—Neg.
12- 9-49 Kahn—Neg. Kline—Neg.
11-10-49 Blood Phenol—Negative

was done until 1941, four years after the patient's mother expired. At that time the lawyer's I.V. pyelogram indicated to us that he had polycystic kidneys. His blood pressure in the three year interval was normal and then in 1941 his blood pressure began to rise and it was systolic 150 with a diastolic of 90. The blood pressure kept on increasing to the higher levels gradually until July, 1947 when I was called to see him at another hospital because of a cerebral hemorrage with a right hemiplegia. We transferred him to Mount Sinai Hospital. Following that, and knowing that he had polycystic kidneys, we watched him and found that he had an enlargement at least of the left kidney in 1947. This gradually kept increasing in size until his admission to the hospital on October 19, 1949. He had this very large mass that was not only palpable but visible. It was nodular and cystic in character and filled up the entire left side of the abdomen and extended beyond the midline in the pelvic region. He was in the hospital for two months prior to his death. He ran the typical course of polycystic kidneys and died at the age of 43. He developed hypertension gradually, which is characteristic, and then the arteriosclerosis with a cerebral hemorrhage, and later on coronary sclerosis. We got an electrocardiogram before he died, when he had precordial pain, and it showed a myocardial infarct. Note the blood chemistry, which is extremely interesting. When he first came in 1947 the non-protein nitrogen was 62 and 77. On the second admission three years later, it varied from 234 to 396. The urea nitrogen ranged from 154 to 280. His creatinine varied from 10.3 to 16.4. During the entire two months, he never actually was in uremia. He was fully conscious and never had any convulsions or twitchings. His eyegrounds,

although showing sclerotic vessels, presented no hemorrhages. He had no headaches and was mentally clear until the day before he died, when he became confused. In the entire two month period, with the extremely high NPN, urea nitrogen and creatinine, he never showed indications of going into uremia, until the day before he died. You recall recently Dr. Davidsohn showed us a man with polycystic kidneys that had very little functioning tissue, who lived to be 85 years old. This patient was in coma the day he was admitted to the hospital; he did show some signs of mental changes for about a six month period. Our patient entered the hospital on 10-19-49 and we know, of course, that his blood chemistry was high even before he was admitted to the hospital, so for at least two months he had extremely high nitrogen retention without going into uremia. He showed no signs of mental changes until the day before he died. His brother, the dentist, 39 years old, was in a hospital last year with a coronary thrombosis; he was in the hospital six weeks, was in shock twice, came out of it and is back in practice today. One of the two sons developed polycystic kidneys and the other one, coronary sclerosis. The dentist and his 12 year old child had I.V. pyelograms taken in 1941 and no polycystic kidneys were found in either at that time. The lawyer had the polycystic kidneys and the dentist did not.

Dr. J. Freilich: I'd like to say just a word about the myocardial infarct that this patient had while he was in the hospital. It occurred during the course of a blood transfusion that he was receiving for the anemia, and the question, of course, of a causal relationship between the blood transfusion and the infarct was brought up. He received about 350 cc of blood, at which time he began to have severe chest pain, the typical pain of an infarct, following which he had electrocardiographic evidence of myocardial infarction. The question is whether this was due to the volume of fluid, to the excitement of the transfusion, or other factors that we can't account for at the present time. One possibility that occurred to me for which there is no evidence that I know of, is the fact that while he was receiving the transfusion he complained bitterly of pain at the site of the venepuncture, and questioned whether the needle had a hook on it, whether it was a dull needle, or whether it entered in a peculiar manner. The question entered my mind as to whether there was some possibility of reversal of the nervous pathways which we see with coronary spasm, that ordinarily gives pain in the left antecubital fossa. Perhaps in some way his reflex could work backwards, the pain in the left arm giving him a reflex coronary spasm with resulting myocardial infarction. Of course, in that case we wouldn't expect to see a thrombosis or embolus in the coronary artery. It is a picture of infarction due to coronary insufficiency.

Dr. Isaacs: This first graph was taken on his first admission in 1947 and beyond a slight flattening of the ST segment and a little depression in lead 3, there is very little abnormality in this graph. The next one was taken on his second admission in 1949. I don't know how close it was to the time of his pain, but there is flattening and depression of ST in 1; there is a definite wide, large abnormal Q wave in leads 2 and 3 and in lead AVF. There is a slight elevation of the ST segment in both leads. There is some flattening of T in V6 and the T in V4 is upright. This is pretty definitely diagnostic of a recent posterior wall infarct. I believe the next graph was taken a few days later, there are very insignificant changes between this, the preceding one and all the following ones. There is a little less elevation in the ST segments here, but otherwise there is no remarkable change. The only additional change was the inversion of T minutely in V4 and you'll notice that the T in V6 is slightly upright. The next one was taken about a week later. This is essentially the same as the one before which may indicate stabilization although it is somewhat early for it. It appears more likely that since this has been such an extensive infarct, the muscle is essentially dead and there has been no further progression. Thus it didn't go through the usual series of changes that one expects

an infarct to go through. This was taken in December, about one month after the others. It shows a little flattening in the ST segments of leads 2, 3 and AVF. The Q wave and the T wave are about as before, perhaps not quite as deep. There are minute changes in the chest leads. The T waves in V4 and V6 are a little bit diphasic. Posterior wall infarct, apparently completely transmural with necrotic muscle.

Dr. H. Kamin: I just noticed the last electrocardiogram showed an inversion of T1 also, in addition to T2 and T3. We have a case of kidney damage, renal failure, with inversion of all the T waves. We should also consider the possibility of pericarditis as well as an infarction.

Dr. Arendt: The diagnosis of polycystic kidney was made, and there is hardly any doubt that is correct. This is a film of the stomach. There is pressure on the stomach from behind, and then, in addition to the pressure, we see the entire mass going down, and there is displacement of the small bowel. The tumor reaches all the way down, to the midline and almost beyond the midline. We see also that there is pressure upon the duodenum. There is a very abnormal duodenal pattern, and we see pressure on the other side. The pressure on the duodenum is either from an enlarged liver or from kidney enlargement. In the next film we see masses on both sides that would very well go with polycystic kidneys. There is bilateral pressure all the way down that ends with the duodenum almost in vertical position on both sides between two walls. The tumor mass extends far down, yet still preserves something of the kidney shape. Otherwise we would have to think of pancreatic cyst in the differential diagnosis. Pancreatic cyst is usually more round, located more medially, and does not usually grow to that tremendous size. The lateral view shows the tremendous mass, beginning retroperitoneally, extending all the way down and displacing the duodenum and stomach.

Dr. I. Davidsohn: I am interested in Dr. Freilich's suggestion that there may be a relation between the blood transfusion and the myocardial infarct. As far as the abstract of the history indicated, there was no evidence for such a relationship. It was stated that during the transfusion after the patient had received 350 cc. of whole blood, he developed pain in the chest. Thrombosis may occur during a transfusion in one of two ways: (1) it may be brought on by a slight but sudden increase in blood pressure with hemorrhage into the intima, especially in severe arteriosclerosis which this patient had; (2) it may be produced by a sudden drop in blood pressure caused by giving too much blood in too short a time in the presence of damaged myocardium. Therefore, I think it important to give the blood very slowly in these patients. One should reduce the speed to one half cc. per minute per pound of body weight when giving a blood transfusion to a patient with myocardial damage. If a patient weighs 140 lbs., the usually recommended rate, unless speed is indicated, is 1 cc. per pound of body weight per hour, or 140 cc. in one hour or a pint in about 3 hrs. In a patient in whom one has reason to suspect cardiac embarrassment, it is advisable to reduce the rate to one half cc. per pound of body weight per hour, thus avoiding the sudden rise in blood pressure and overloading the heart.

Postmortem Findings

Dr. I. Davidsohn: This patient's heart was not enlarged as one would expect in this type of hypertension. It weighed only 330 Gm. The left ventricle was distinctly dilated with marked thinning of the walls. In the posterior wall of that chamber there was an area of hemorrhagic and yellowish discoloration with softening, which on section represented acute myocardial infarction with necrosis. The heart valves were normal. There was marked sclerosis of the coronary arteries with a thrombus in the right coronary artery about 3-4 cm. from the orifice. Microscopic study of sections of the myocardium showed in addition to the acute infarction, evidence of the old healed infarcts.

The kidneys were tremendously enlarged, weighing together 6100 gm. which is about 25 times the normal weight of

the kidneys for a person of that age. The enormous kidneys were composed of a great many cysts. Section of the kidneys after fixation revealed multiple cysts varying from 0.5 to 5 cm. in greatest dimensions, some of them filled with hemorrhagic material, and showed very little functional parenchyma, although enough remained to sustain this patient for a long time as Dr. Freilich brought out. The evidence of renal failure came rather late because of the immense size of the kidneys; even if only a relatively small amount of functioning parenchyma remained, there was enough to sustain life for a long time. On microscopic examination there were numerous thin-walled dilated cysts separated by islands of atrophic and fibrotic glomeruli and dilated tubular elements in a stroma infiltrated with chronic inflammatory cells and presenting interstitial hemorrhages. Many glomeruli showed adhesions between the capillaries and Bowman's capsule and hyaline thrombi within capillaries. The wall of the renal artery was thickened by arteriosclerosis. There was marked atheromatosis of the aorta. Changes that have been described in cases of uremia were found in several organs such as the pituitary gland, the parathyroids, and pancreas.

In the pituitary there were increased numbers of basophilic cells with only occasional eosinophilic and chief cells. Basophilic hyperplasia has been described in cases of uremia.

There was also hyperplasia of the parathyroid glands, with marked enlargement of two of them to 1 cm. in diameter each. Microscopically, they showed areas of hyperplasia of the chief cells and areas of hyperplasia of the water-clear (wasserhelle) cells, the latter being a frequent feature of parathyroid hyperplasia. There were also more glandular appearing areas, the so-called pseudo-glands, lined by water-clear cells. A result of this parathyroid hyperplasia was deposition of calcium in various organs, so-called calcium transport. There were massive deposits of calcium in the kidney and in the myocardium.

In the pancreas the acini were markedly dilated and filled with inspissated material corroborating a recent observation by Baggenstoss in cases of uremia. This lesion is not specific for uremia but is frequently present in this condition. I have also seen it in ulcerative colitis. It seems to be present in cases with severe dehydration.

In the presence of cystic disease of the kidneys one should always suspect the occurrence of cysts in other organs. In this case multiple cysts were found in the liver, which on microscopic examination proved to be distended bile duct cysts lined with cuboidal epithelium.

An additional finding was an old cerebral lesion, a cystic encephalomalacia involving the left basal ganglia and left portion of the pons.

Anatomic Diagnosis: Congenital polycystic disease of the kidneys with dilatation of the renal pelves and intracystic hemorrhages; recent and old myocardial infarcts of the posterior wall of the left ventricle; thrombosis of the right coronary artery; severe arteriosclerosis of the coronary arteries and aorta; hyperplasia of the parathyroids; hyperplasia of basophilic cells of the pituitary; pancreatic stasis; cystic encephalomalacia of the brain; multiple biliary cysts and cavernous hemangioma of the liver with chronic passive congestion; chronic passive congestion of the spleen; organizing pneumonia of the lungs; old left pleural adhesions; uremic frost of the skin; bone marrow hypoplasia.

Cause of death: Recent myocardial infarcts due to coronary artery thrombosis and uremia due to congenital polycystic disease of the kidneys.

Summary and Comment

The unusual features of this case are:

1. The extreme involvement of both kidneys with transformation of the organ into a huge mass of cysts. The immense reserve power of the kidney is illustrated by the fact that the patient was able to get along on a relatively small amount of functioning renal parenchyma.

2. The hyperplasia of the parathyroids so frequently mentioned as present in chronic renal failure is seldom seen reaching the proportions of this case.

3. The same is true for the basophilic cell hyperplasia in the pituitary gland.

4. The duration of and stasis of secretion in the excretory ducts of the pancreas is in keeping with recently reported observations.

5. The association of cystic disease of the liver and kidney is also clearly shown.

Correlation of clinical and pathologic findings. All clinical manifestations and clinical laboratory findings are fully explained by the autopsy findings. The cystic encephalomalacia in the left basal ganglia and pons are the final changes resulting from the cerebro-vascular accident recorded in the history as having occurred two years prior to death.

BIBLIOGRAPHY.

Lambert, P. Q.: Polycystic Disease of the Kidney. Arch. Path. **44**: 34 (1947).

Albright, F. and Reifenstein, E. C.: Parathyroid Glands and Metabolic Bone Disease. Baltimore, 1948. The Williams and Wilkins Company.

Fishberg, A. M.: Hypertension and Nephritis. Philadelphia, 1939, Lea and Febiger.

Bell, E. T.: Cystic Disease of the Kidneys. Am. J. Path. **11**: 373-418 (1935)

McKenna, C. M. and Kampmeier, O. T.: A Consideration of the Development of Polycystic Kidney. Tr. Am. A. Genito-Urin. Surgeons. **26**: 377-383 (1933).

Baggenstoss, A. H.: Dilatation of the Acini of the Pancreas Incidence in Various Pathologic States. Arch: Path. **45**: 463-473 (1948).

Pictures of Specimens

Fig. 1. Kidney 3000 Gm. (N. 140 Gm.); Polycystic Disease. The organ is composed of a series of thin walled dilated cysts, some of them containing hemorrhagic material.

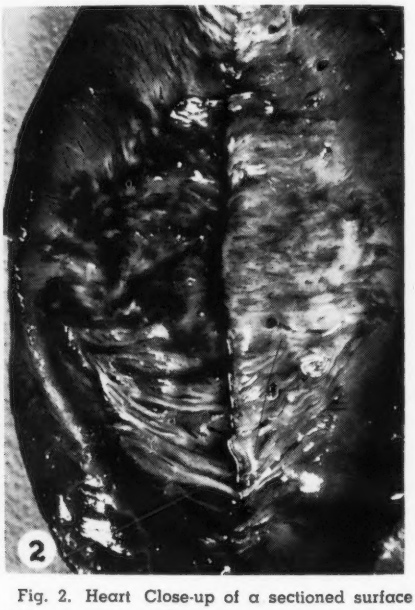


Fig. 2. Heart Close-up of a sectioned surface of the posterior wall. On this cut section is seen the softened area of hemorrhagic and yellowish discoloration of the myocardium, indicating an acute infarct. This lesion was a major factor in causing the death of this patient.

Fig. 3. Parathyroid glands. In this photograph there is an increased number of the water-clear cells, some of them in the form of pseudo-glands. This is another result of a uremic condition. Parathyroid hyperplasia may lead to deposition of calcium in various organs. Photomicrograph X 170.

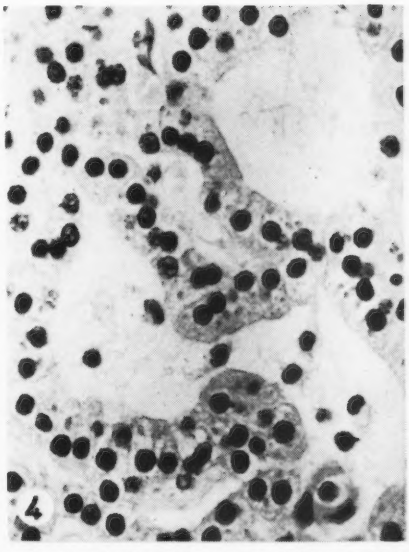


Fig. 4. Parathyroid glands. With the higher magnification photomicrograph the acinar arrangement of the water-clear cells and their detailed structure are better seen. Photomicrograph X 500.

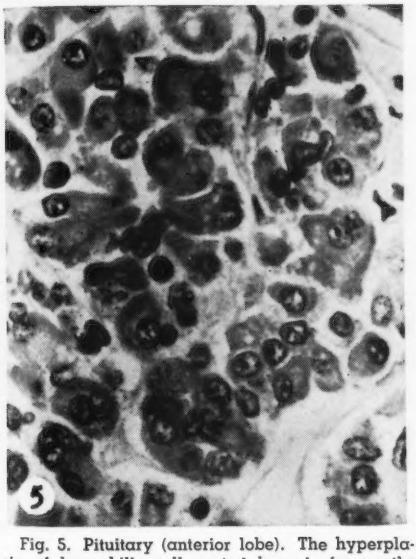


Fig. 5. Pituitary (anterior lobe). The hyperplasia of basophilic cells noted here is frequently described in uremia. Photomicrograph X 500. Larger cystic cavities are lined with low cuboidal epithelium.

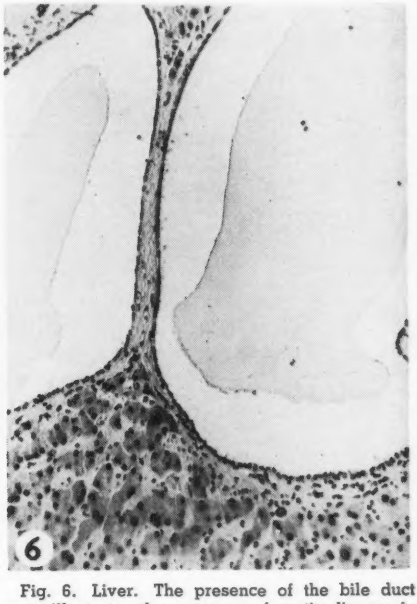


Fig. 6. Liver. The presence of the bile duct cysts illustrates the presence of cystic disease in other organs besides the kidneys. Photomicrograph X 120.

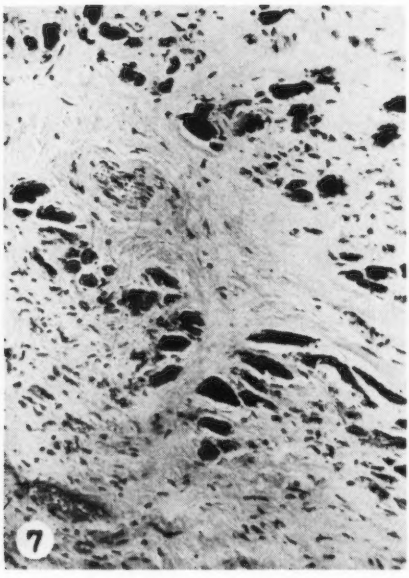


Fig. 7. Heart. The black clumps are deposits of calcium demonstrated with a special stain (Von Kossa). The presence of calcium transports in the myocardium is the result of mobilization of calcium by hyperactivity of the parathyroid glands. Photomicrograph X 120.

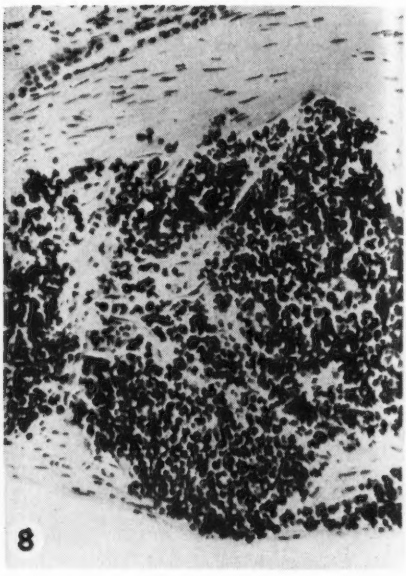


Fig. 8. Kidney. Focal deposits of calcium in the kidneys are also the consequence of hyperparathyroid activity. X 120.

BOOK REVIEWS

DISEASES OF THE HEART AND CIRCULATION by Paul Wood, O.B.E., M.D., F.R.C.P. 590 pp. 355 figures. $12.50. J. P. Lippincott Company, Philadelphia.

This book, written by the director of the Institute of Cardiology, London, presents a study of heart disease as it is expounded in Great Britain and the Continent. As such it encompasses a refreshing and stimulating discussion of the most modern concepts of cardiac disease. The arrangement of the contents has been determined chiefly by physiological and etiological considerations, rather than by morbid anatomy. Thus there are no chapters devoted to valvular disease as a whole, nor to diseases of the myocardium. There is an excellent chapter entitled "Approach to Cardiology," in which the author explains in detail the special tests used in cardiac study — circulation time, cardiac catheterization, cardiac output, arterial oxygen saturation, vital capacity, jugular phlebogram, arteriography, phonocardiography and ballistocardiography. The last chapter is devoted to a discussion of disturbances associated with psychiatric cardiovacular states. The index also serves as a guide to differential diagnosis. The printing and binding are excellent. The book should be in the medical library of all physicians and students who are interested in clinical cardiology.

* * *

NASAL SINUSES by O. E. Van Alyea. M.D. Cloth. Second edition. 327 pages with 143 illustrations. Baltimore. The Williams and Wilkins Company. 1951. $9.00.

This book is an excellent treatise on the nasal sinuses. It is well organized, amply illustrated and clearly written. The author has presented a great deal of clinical material with accompanying embryologic, histologic and pathologic background. The chapter on the physiology of the nose, however, was short and somewhat incomplete. The closing chapter deals with general therapeutic measures and is up to date with respect to current views on the use of antibiotics systemically and locally. Several case reports are included to illustrate topics under consideration. They are presented directly and in interesting fashion. There is an instructive chapter on sinus disease in children. The author forcefully points out that these conditions must be appreciated, properly diagnosed and treated. Extensive bibliographic material is included in each chapter. The book is highly recommended for otorhinolaryngologists and general practitioners.

* * *

METABOLIC METHODS by C. Frank Consolazio, Robert E. Johnson, and Evelyn Marek. Cloth. First edition. 471 pages with 65 illustrations. St. Louis: C. V. Mosby Company, 1951. $6.75.

This new book is a rather complete presentation in detail of the commonly used laboratory procedures in metabolic studies and in routine analyses of tissues, foods, and body fluids. The most practical methods currently in use are presented, and for this reason isotope, electrophoresis, and ultracentrifuge techniques are not included. Original references are included for each procedure and detailed references ar listed for the more recent methods. The book is recommended for a reference text to research and laboratory workers and practitioners interested in carrying out laboratory work.

* * *

EVALUATION OF THE PELVIS IN OBSTETRICS by Howard G. Moloy, M.D., M.Sc. Paper. 119 pages, 68 figures. Philadelphia and London: W. B. Saunders Company, 1951. $2.50.

This book is the first of a series in which the publishers have economized on printing and binding in order to make valuable medical information available at low cost to students, interns, residents and others. The type is very legible and the figures are clear. The cover, however, is not at all substantial. Dr. Moloy, an authority on pelvimetry, has presented a monograph on the general morphology of the pelvis, its clinical examination, forceps operation, breech delivery, roentgenologic technique, and methods for quantitative estimation of cephalopelvic disproportion. He deals extensively with the classification of pelves and their clinical importance. The book should be of value to obstetricians, but is rather advanced for students.

* * *

CLINICAL LABORATORY METHODS by W. E. Bray, M.D. Cloth. Fourth edition. 614 pages with 119 illustrations and 18 color plates. St. Louis: The C. V. Mosby Company, 1951. $7.25.

Dr. Bray's most recent revision of this book has resulted in a superior laboratory manual which embraces all the procedures of modern clinical laboratory medicine. In addition to the routine examination of urine blood, feces, etc., there are excellent chapters on laboratory bacteriology, mycology, poisons and surgical pathology. Antibiotic assay, Papanicolaou staining, virus agglutination technique, and adrenal hormone assay are among the many new methods which are included. The color plates and figures are excellent, but the print is small and uneven. The book is recommended for students and physicians.

* * *

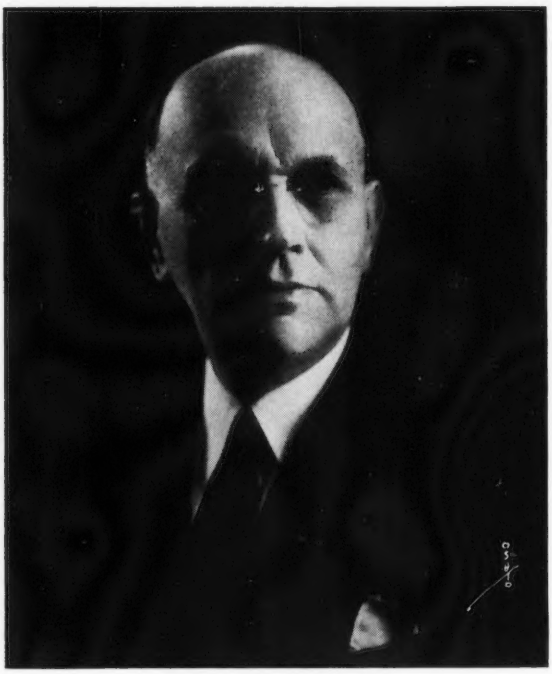
IMMUNOLOGY by Noble Pierce Sherwood, Ph.D., M.D., F.A.C.P. Third edition. Illustrated. C. V. Mosby Co., St. Louis, 1951. 731 pp. $8.00.

The third edition of this book remains a definitive text for those who are interested in the underlying principles involved in infection, resistance and diagnostic laboratory tests. Emphasis has been placed throughout the book on changing points of view relative to natural and acquired immunity and allergy. Among the new topics discussed are new blood group factors, latent infection, mechanism of viral infection, the role of vertebral veins in metastasis, and the new concepts relative to the role of vitamins and endocrines in resistance. A new chapter dealing with the Rh and Hr factors has been added. There is a lucid chapter on colloid chemistry which seems to explain some of the processes involved in agglutination opsonification and complement fixation. Readable print and 7 color plates serve to enhance the value and appearance of this text. This book is invaluable for medical students and practitioners who wish to understand the fundamental mechanisms of immunology.

* * *

A TEXTBOOK OF THE PRACTICE OF MEDICINE, by Various Authors. Edited by Frederich W. Price. Eighth Edition, Geoffrey Cumberlege, Oxford University Press, New York, 1950. $9.00.

The eighth edition of this popular textbook contains many necessary additions and revisions. Altogether there are 31 contributors from the British Isles. New articles have been added on rehabilitation of paraplegics, filaria blastomycoses, Reiter's disease, chronic intermittent juvenile jaundice, paroxysmal proctalgia, cervical intervertebral disc, calcified pericardium, diaphragmatic hernia and atomic injuries. There is nothing on the newer antibiotics such as aureomycin, chloramphenicol (chloromycetin) and terramycin nor are cortisone and ACTH mentioned. The book is well organized and adequately indexed. The work is as good as several of the books on internal medicine in this country and should prove useful to students and practitioners alike.



BRUCE WESLEY DICKSON
Died September 1, 1951

It is with deep regret that we announce the death of Mr. Bruce Wesley Dickson, Registrar of The Chicago Medical School for the past sixteen years, on September 1, 1951, at the Woodlawn Hospital in Chicago. Respected as an associate by the faculty and admired as a friend by the students, Mr. Dickson played a significant and integral part in the development of The Chicago Medical School.

Born in Kingsport, Tennessee, Mr. Dickson received the Bachelor of Arts degree from Carson Newman College in Jefferson City, Tennessee in 1906 and the Master of Arts degree from the University of Arkansas in Little Rock in 1912. While at the University of Arkansas, he received a teaching fellowship and in 1915 he took further instruction at Yale University. He then transferred to the University of Chicago, and in 1916 the degree of Master of Arts was conferred upon him by the Divinity School.

In 1917 he was appointed Office Manager of the Central Young Men's Christian Association in Chicago. Choosing to ally himself more closely with the problems of student life, he was appointed advisor to the foreign students of the University of Chicago in 1920. Anxious

to aid in the adjustment of students from other countries, Mr. Dickson in 1923 began negotiations with Mr. Rockefeller and his associates for the establishment of some central agency for the orientation of the foreign students. Through these joint endeavors the International House at the University of Chicago became a reality. In 1931 Mr. Dickson was rewarded with the position of Director of International House, which he held until 1935.

In that year he was appointed Registrar of the Chicago Medical School, and focused his attention, along with the other members of the staff, on the improvement of the school. His cooperation with the various committees and his friendliness towards the students endeared him to both these groups.

The administration, members of the faculty and the student body join in expressing their condolences to Mr. Dickson's survivors: his widow, Mrs. Marjorie H. Dickson, his son, Bruce Wesley Dickson, Jr., and his daughter, Miss Nan Dickson.

* * *

Dr. A. H. Ryan, Dean of Students, has announced that 1,670 applications have been received for the 72 available positions in the entering Freshman class. Among those desiring to initiate their medical careers at The Chicago Medical school were applicants from every state in the Union with the exception of Montana and New Mexico. In addition, applications were received from eleven foreign countries.

Of the successful applicants all have received Bachelor's degrees. Of these 17 have Master's degrees and one, a Doctor of Philosophy. Represented in this class of 1955 are students from 37 Colleges and Universities, coming from 15 states. Seventeen veterans are among the members of this class.

FACULTY NEWS

Dr. F. J. Mullin, Dean of the Faculty, has been named chairman of the newly formed National Inter-Association Committee on Internships. This is a central clearing body that will put into operation a plan proposed by Dr. Mullin for arranging internship appointments by matching preference of students with preference of hospitals.

The Committee is composed of representatives from the American Hospital Association, American Protestant Hospital Association, the Catholic Hospital Association, Association of American Medical Colleges, Council on Medical Education and Hospitals of the American Medical Association, and liaison members from the Air Force, Navy, Public Health Service and Veterans Administration which are the Federal agencies offering internships.

Department of Anatomy

The Dr. M. L. Parker Award for meritorious scientific research during the academic year 1950-51 was presented to Dr. George Clark, Associate Professor of Neuro-Anatomy, at the Commencement Exercises on June 23, 1951.

Dr. Hans Elias, Assistant Professor of Microscopic Anatomy, recently presented a paper before the Chicago Society of Pathologists.

A research grant of $5,635 has been made by the Public Health Service of the Federal Security Agency to Dr. Harold Koenig, Assistant Professor of Anatomy. Dr. Koenig's research project is a morphologic and quantitative study of nucleoprotein in developing nerve cells grown in tissue culture.

Department of Biochemistry

Dr. A. Robert Goldfarb recently spoke before the Pharmacology Seminar of Loyola University and the Graduate Chemistry Group of the University of Illinois.

Department of Dermatology and Syphilology

Dr. David Cohen, Professor and Acting Chairman of the department, presented one of a series of lectures at the recent Mount Sinai Health Forum.

Department of Microbiology and Public Health

Dr. Harold Elishewitz, Assistant Professor of Parasitology, recently spoke before the Chicago Cancer Research Group and the Midwestern Conference of Parasitologists held at Purdue University.

Dr. Paul H. Kopper, Assistant Profes-

sor of Microbiology and Public Health, presented a paper at the annual meeting of The Society of American Bacteriologists held at the Edgewater Beach Hotel, Chicago, Illinois. Dr. Kopper has also published an article in the Journal of Physiology, Vol. 34, No. 5.

Dr. George J. Scheff, Assistant Professor of Microbiology and Public Health, spoke before The American Academy of Tuberculosis Physicians at their annual meeting at Atlantic City. The Chicago Heart Association has awarded a grant of $4000 for research to be conducted by Dr. Scheff.

Department of Medicine

Dr. Aldo A. Luisada, Associate Professor of Medicine and Program Director of Cardiology, acted as moderator for a panel discussion of the American Society of Chest Physicians at the annual Heart Convention held recently in Atlantic City. Grants totalling $8,800 have been presented by the Chicago Heart Association to Dr. Luisada for studies to be conducted under his direction.

Dr. Manuel G. Spiesman, Associate Professor of Medicine, presented lectures before the Hospital Militar, Havana, Cuba and the International Academy of Proctology, Atlantic City.

Department of Neurology and Psychiatry

Dr. Louis Berlin, Associate in Neurology, has recently presented a lecture at The Michael Reese Hospital.

Department of Obstetrics and Gynecology

Dr. Walter J. Reich, Assistant Professor of Gynecology, and Dr. Mitchell J. Nechtow, Assistant Professor of Obstetrics, have had articles published in the American Journal of Obstetrics and Gynecology, Vol. 61, No. 6 and The Mississippi Valley Medical Journal, Vol. 73, No. 3.

Department of Orthopedic Surgery

Dr. Donald S. Miller, Professor and Chairman of the Department of Orthopedic Surgery, has been elected Vice-President of the Chicago Orthopedic Society for the coming year.

Department of Pathology

Dr. Israel Davidsohn has presented two lectures before the Armed Forces Institute of Pathology, Washington, D. C. Dr. Davidsohn has also been elected President of the Illinois Association of Blood Banks.

Dr. Abe Oyamada, Associate in Pathology, has been awarded the Ruth Berger Reader Fellowship in the amount of $1,500 for research on hemolytic anemias. This is the second year that this fellowship has been awarded to Dr. Oyamada.

Dr. Israel Davidsohn, Dr. Kurt Stern and Dr. A. C. Ritchie addressed the Chicago Cancer Research Group at a recent meeting.

Dr. A. C. Ritchie, graduate of the University of Otago, Auckland, New Zealand and Oxford University, England, has arrived in this country as a visiting member of the faculty. Dr. Ritchie, who taught Pathology at the University of Oxford for several years before coming here, will work in the Laboratory of Cancer Research under the direction of Dr. Philippe Shubik, Assistant Professor of Surgery and Coordinator of the Cancer Teaching Program.

Department of Pediatrics

Dr. Emanuel Padnos, Assistant Professor of Pediatrics has published an article in The Journal of Pediatrics, Vol 38, No. 1, with the aid of Dr. Milton Goldin.

Department of Physiology

Dr. Piero P. Foa, Professor of Physiology, has been awarded a grant of $6,000 by the Eli Lilly Research Laboratories for work in experimental diabetes.

Department of Surgery

Dr. David Movitz, Dr. Leo Zimmerman and Dr. Edward S. Warnick were awarded the Bronze Medal "for most original work" in an exhibit on "The Use of Arteriography in the Diagnosis of Peripheral Vascular Diseases" shown before the Illinois State Medical Association's 111th Annual Convention on May 22-24, 1951.

This exhibit was also presented at The Chicago Medical School Alumni Week meeting.

Dr. Philippe Shubik, Assistant Professor of Surgery and Program Director of Oncology, has recently published an article in Vol. 11, No. 5 of Cancer Research.

ALUMNI NEWS

Class of 1935

Dr. Abe I. Podolsky has been appointed Second Vice President of the Board of Medical Examiners of the State of Arizona.

Class of 1937

Dr. Norman S. Angel has recently opened an office in Miami, Florida.

Dr. Edgar O. Breakstone has been certified by the American Board of Otolaryngology.

Class of 1938

Congratulations to Dr. and Mrs. George E. Fisher on the birth of a son, Byron, on June 6, 1950. Dr. Fisher has also received his Reciprocity License in Missouri and is now at the O'Reilly Veterans Hospital, Springfield, Missouri.

Congratulations to Dr. and Mrs. Hannibal Paolozzi on the birth of a daughter, Mary Beth, on May 21, 1951.

Class of 1941

Dr. Edwin I. Hirsh has been certified by the American Board of Radiology.

Class of 1942

Dr. Allen W. Jackman is now on the staff of the Community Clinic at Maywood, Illinois.

Class of 1943

Dr. Eugene Raicus has been elected an Associate Fellow in the International College of Surgeons.

Dr. Frank I. Uyeno has been appointed Resident in Psychiatry at the Eastern State Hospital, Medical Lake, Washington.

Class of 1944

Congratulations to Dr. and Mrs. Bernard Tumarkin on the birth of a son, Paul Robert, on August 3, 1951.

Dr. Burton J. Winston has just completed a post-graduate course in cardiology at the Harvard Medical School.

Class of 1945

Dr. Lawrence Gluckman has been commissioned a Captain in the Army Medical Corps, and is now *en route* to Korea.

Class of 1946

Dr. Louis J. Polskin, now a Captain in the Army Medical Corps, has recently been assigned to the Medical Nutritional Laboratory, Chicago, Illinois.

Dr. James Weishaus has been certified by the American Board of Psychiatry and is now at the Brentwood Veterans Administration Neuropsychiatric Hospital, Los Angeles, California.

Class of 1947

Congratulations to Dr. and Mrs. Jerome A. Ehrlich on the birth of a daughter, Amy Beth, on August 7, 1951.

Congratulations to Dr. and Mrs. Samuel Weinberg on the birth of a son, Ronald Andrew, on June 19, 1951. Dr. Weinberg has been commissioned as Captain in the U. S. Air Force Medical Corps and is now Base Pediatrician at the March Air Force Base, California.

Class of 1948

Dr. Joseph Barnett has accepted an appointment as Senior Resident in Psychiatry at the Syracuse Psychopathic Hospital, Syracuse, New York.

Congratulations to Dr. and Mrs. Wallace L. Salzman on the birth of a son, David Julius, on June 24, 1951.

Class of 1950

Dr. James R. Carey has been commissioned a First Lieutenant in the Army Medical Corps and is now serving with the Sixth Army.

Congratulations to Dr. David Katz on his marriage to the former Miss Janet Kane of Chicago on June 7, 1951.

Congratulations to Dr. and Mrs. Jerome Z. Litt on the birth of a daughter, Erica Susan, born July 17, 1951.

Dr. Milton Miller has been elected President of the Cook County Hospital Interne Association.

Congratulations to Dr. and Mrs. J. Marvin Wertheim on the birth of a son, Wayne Howard, on June 26, 1951.

Class of 1951

Lawrence Berger received the John J. Sheinin Meritorious Award for excellence of character, scholarship and professional competence at the 37th commencement exercises of The Chicago Medical School.

STUDENT NEWS

Class of 1952

Congratulations to Norman Blass on his marriage to the former Miss Lucille Greenberg, of Chicago, on September 16, 1951.

Best wishes to Herbert S. Radley on the announcement of his engagement to Miss Charlene B. Wilder of Chicago.

The officers of the Class of 1952 for the senior year were elected. They are:

David Schulman ..... President
Lloyd Paul ..... Vice-President
Marion Finkel ..... Secretary
Eugene Fierer ..... Treasurer
Stuart Cohn, Sanford Cohen—
Student Council Representatives

Committees were established to facilitate the activities of the Senior year. Harold Ratner was appointed Chairman of these committees.

ORGANIZATION NEWS

Phi Delta Epsilon

The Beta Tau Chapter of Phi Delta Epsilon anticipates a full calendar of events for the forthcoming school year. A smoker will be held at the University of Illinois Student Union during the first week of the quarter in order to introduce the members of the Freshman Class to the faculty, and to fellow students.

Late in the Fall Quarter, Phi Delta Epsilon will continue its policy of sponsoring programs of an informative and educational nature. There will be speakers, films, and other sundry activities designed to broaden the student's insight into medicine. In the winter, the gala Annual Initiation Banquet and Dance will be held in conjunction with the other Chicago chapters of the fraternity. This is an affair looked forward to with great eagerness by members and pledges of Phi Delta Epsilon.

The John J. Sheinin Lectureship Series will continue to present eminent personalities in the field of medicine. This year, Dr. William Dameshek of Boston discussed "The Spleen and Hypersplenism."

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Phi Lambda Kappa

The Alpha Rho Chapter has made extensive plans for the coming school year. Pledging affairs, lectures, trips, seminars, dances and other social events are all included in our proposed program. A series of lectures on "Marriage" has been instituted this fall. Prominent faculty members will discuss various phases of this topic during monthly business meetings. The first lecture, delivered by Dr. Hilkevitch of the Department of Psychiatry, dealt with "Marital Relations." The climax of the fall and winter activities will be the third annual Maurice Oppenheim Lectureship which will be delivered this year by a world-renowned medical scientist.

Phi Lambda Kappa welcomes the newly arrived freshmen. We hope your stay at C.M.S. will be both fruitful and enjoyable. We offer our hand to assist our new fellow students in any way possible and we want all of you to feel free to call upon any of the fraters for any assistance you may need.

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Association of Interns and Medical Students

The A.I.M.S. fall program began on Wednesday, October 3, 1951, when Dr. Peter Gaberman, faculty advisor of the A.I.M.S. and Associate Professor of Medicine at The Chicago Medical School, spoke to the new freshmen.

All A.I.M.S. chapters are preparing for the National A.I.M.S. Convention which will be held at the Illini Union Building, starting Wednesday, December 26, 1951, and ending Sunday, December 30, 1951. Since this is the time when A.I.M.S. policy for the coming year is decided upon, all members who can come, should be there.

Our chapter is in charge of the Publicity Committee for this convention. All those who would like to help are asked to see Ed Weismann, chairman.

Other news of national interest is the announcement that "The Interne," the official publication of A.I.M.S., will again be published.

Finally, A.I.M.S. is happy to announce that Dr. P. Foa, Associate Professor of Physiology at The Chicago Medical School, is the newly selected Faculty Advisor of A.I.M.S. Dr. Peter Gaberman, Associate Professor of Medicine at

The Chicago Medical School, is the other Faculty Advisor.

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Student American Medical Association

The Student American Medical Association has moved beyond the organization stage here at The Chicago Medical School and other medical schools throughout the country. Our chapter, as a charter member, has joined in this active plan to bring new benefits to the medical student and future physician.

In January, the nation's 35,000 medical students and interns will receive the first issue of the Journal of the Student American Medical Association. Included in this issue will be scientific articles; information to medical students, interns, and residents; a history of medicine series; and true medical experiences. The journal will be published 9 months of each year by the SAMA.

The Association's future plans include: (1) the establishment of a nation-wide hospital and surgical insurance plan in cooperation with the medical schools, which would cover medical students not only during the school year, but during summer and other vacation periods; (2) the establishment of a clearing house for summer jobs and the arranging of research opportunities, field studies, and special summer scientific training; (3) the dissemination of up-to-date information regarding medical curricula, together with proposed additions or deletions in the curricula of medical schools; (4) the sponsorship of scholarships and possibly a year of advanced study for outstanding medical students and (5) the establishment of exchange programs in cooperation with other foreign student medical associations.

EDITOR'S NOTE

With this first number of Volume 13, The Chicago Medical School QUARTERLY embarks upon a new phase of its growth and development. Eight more pages have been added per issue to make a total of one hundred ninety-two pages per volume. In the past several years, the QUARTERLY has assumed a responsible position in the current medical literature, as evidenced by its greatly increased circulation and its favorable reception by medical libraries and universities throughout the world. The Editorial Staff has attempted to strike a balance in articles selected for publication so that material published would be of interest to the clinician, research worker and student of medicine alike. We believe that we have made noteworthy strides in this direction and will endeavor in future issues to further enhance the value of the QUARTERLY to its readers. It is our desire to encourage our alumni to submit articles dealing with subjects of general interest to their colleagues, descriptions of research projects they may be engaged in and case studies in which they have participated. We promise them our fullest co-operation in this regard.

Among the new innovations in the Features Department will be the printing of abstracts of all articles published by members of the faculty, alumni or students in the various medical journals. However, in order for this project to achieve success, it will be necessary for the aforementioned authors to submit to the QUARTERLY an abstract of their article of approximately 200-300 words in length. Reprints of the original article should accompany the abstract, although this is not necessary. The abstracts should be sent to: The Editor, The Chicago Medical School Quarterly, 710 South Wolcott Avenue, Chicago 12, Illinois. They should be submitted as soon as possible after publication of the article.

It is also requested that the alumni of The Chicago Medical School submit to the QUARTERLY any personal news which would be of interest to the members of their respective classes. Such items as certification by any of the various specialty boards, change of address, appointment to the staff of the various hospitals, election to administrative positions of their medical societies, appointment as residents or senior interns in the various hospitals is included in this division as well as any news of marriages, births and other vital statistics.

The alumnus should include his year of graduation when submitting any of the above material to facilitate its proper classification. Secretaries of the various active organizations in the School are also requested to submit to the QUARTERLY a list of their officers and their activities of the past year, as well as their proposed activities for the coming year.

The cooperation of the above groups will make it possible for the QUARTERLY to present to its readers a more complete coverage of their activities.

NEW BOOKS IN THE LIBRARY

Annual review of medicine. Vol 2, 1951.
Annual review of physiology. Vol. 13, 1951.
Bolivar, S. Selected writings. 2 vols., 1951.
Duncan, G. G. Diabetes mellitus. 1951.
Farr, L. E. Treatment of nephrotic syndrome. c1951.
Feinberg, et al. Antihistamines. c1950.
Gregg, D. E. Coronary circulation. 1950.
Hahn, P. F., ed. Artificial radioisotope therapy. 1951.
Harrison, B. M. Embryology of chick and pig. 3rd ed. c1950.
Hilton, J. Rest and pain. 1950.
Kidd, J. G., ed. Pathogenesis and pathology of viral diseases. 1950.
Marple & Wright. Thromboembolic conditions and treatment with anticoagulants. c1950.
Marshall, M. S. Applied medical bacteriology. c1947.
Meyer, A. W. Rise of embryology. c1939.
Moruzzi, G. Cerebellar physiology. c1950.
Price, F. W., ed. Practice of medicine. 8th ed. 1950.
Pullen, R. LeR., ed. Communicable diseases. 1950.
Rosenbluth, A. W. Transmission of nerve impulses at neuroeffector junctions. c1950.
U. S. Naval Medical School. Color atlas of pathology. n.d.
Yearbook of physical medicine, 1950. 1951.
Advances in carbohydrate chemistry. Vol. 5. 1950.
Altschule, M. D. Physiology in diseases of the heart and lungs. 1950.
Anderson, W. A. D. Synopsis of pathology. 2nd ed. 1946.
Bessey, E. A. Morphology and taxonomy of fungi. 1950.
Burnet & Finner. Production of antibodies. 2nd ed. 1949.
Ciba Foundation. Toxemias of pregnancy. 1950.
Dameshek & Taylor, eds. Symposium on hematology. 1949.
Davis, H. S. Mechanism and evaluation of antiseptics. 1950. (Anna. N. Y. acad. sci., *53*, art. 1).
Eastman, N. J. Williams Obstetrics. 10th ed. c1950.
Gray, J. S. Pulmonary ventilation and ita physiological regulation. 1950.
Janney, J. C. Medical gynecology. 2nd ed. 1950.
Karsner, H. T. Pathology. 7th ed. c1949.
Keefer, C. S. Terramycin. 1950. (Ann. N. Y. acad. sci., *53*, art. 2).
Lederle Laboratories. Aureomycin. c1950. copy 2.
Lee, D. H. K. Physiology of tissues and organs. c1950.
Low-Beer, B. V. A. Clinical use of radioactive isotopes. c1950.
McManus, J. F. A. Medical diseases of the kidney. 1950.
Moench, L. G. Headache. (1948).
Nat'l Board Med. Exam. Examination questions, rev. to Jan. 1, 1951.
Penfield & Rasumssen. Cerebral cortex of man. 1950.
Pohle, E. A., ed. Clinical radiation therapy. 2nd ed. 1950.
Reiss, F. Medical mycology. 1950. (Ann. N. Y. acad. sci., *50*, art. 10).
Scott, J. P. Methodology — techniques for study of animal societies. 1950. (Ann. N. Y. acad. sci., *51*, art. 6).
Sodeman, W. A., ed. Pathologic physiology, mechanisms of disease. 1950.
Stern, C. Human genetics. 1949.
Sumner & Myrback. Encymees. Chemistry and mechanism of action. Vol. 1. 1950.
Sweet, R. H. Thoracic surgery. 1950.
Thomas, J. E. External secretion of pancreas. c1950.
U. S. A. E. C. Atomic energy and physical sciences. 1950.
Abt, L. E. Human engineering. 1951.
A.M.A.A.S. Brief history of the Ass'n. 1948.
A.A.A. Proceedings of anatomists. 63 meeting. 1948.
Argentina. Digesto de salud publica. Vol. 1. 1950.
Armour & Co. Atlas of hematology. 1945.
Auralpan research division. Common infectious diseases. c1949.
Berens & Siegel. Encyclopedia of the eye. c1950.

NEW JOURNALS

Modern medical annual, 1948-1950 (yearly).
Quarterly review of otorhinolaryngology. Vols. 7-8, 1948-49.

Miss M. Campbell,
Librarian.